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THE PATHOLOGY OF THE EYE



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THE
PATHOLOGY OF THE EYE

BY

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VOLUME II
HISTOLOGY.—PART II

LONDON
HODDER AND STOUGHTON

27 PATERNOSTER ROW

1905

*Printed by Adlard and Son,
London and Dorking.*

CONTENTS OF VOLUME II

HISTOLOGY.—PART II

CHAPTER VII

	PAGE
THE LENS	389
The Normal Lens	389
Cataract in General	392
Special Forms of Cataract	398
SENILE CATARACT	398
LAMELLAR CATARACT AND ALLIED FORMS	401
ANTERIOR POLAR CATARACTS	407
ANTERIOR CAPSULAR CATARACT	407
POSTERIOR POLAR CATARACTS	417
TRAUMATIC CATARACT	417
Special Forms of Cataract	
<i>—continued.</i>	
SECONDARY CATARACT	419
FOREIGN SUBSTANCES FOUND IN THE LENS	421
COMPLICATED CATARACTS	421
TOXIC CATARACTS	424
LEPROSY	424
DIABETIC CATARACT	425
CHANGES IN THE SUSPENSORY LIGAMENT	426
CALCIFICATION AND OSSIFICATION	427

CHAPTER VIII

THE VITREOUS	428
The Normal Vitreous	428
Fluidity of the Vitreous	429
Detachment	429
Abnormal Products in the Vitreous	432
INFLAMMATORY PRODUCTS	432
Abnormal Products of the Vitreous—continued.	
TUMOURS, 435 ; BLOOD	435
Parasites	436
CYSTICERCUS, 436 ; ECHINOCOCCUS, 438 ; FILARIE	441
Ossification	442

CHAPTER IX

THE CHOROID

PAGE

443

The Normal Choroid	443	Tumours	489
Wounds and Injuries	445	DERMOID	489
Inflammation	446	MYOMA	490
ACUTE AND SUPPURATIVE	446	ANGIOMA	490
METASTATIC SUPPURATIVE	448	PLEXIFORM NEUROMA	492
SUBACUTE AND CHRONIC	449	SARCOMA	493
CHOROIDITIS DISSEMINATA	458	CLASSIFICATION, 493; FRE-	
SYMPATHETIC CHOROIDITIS	460	QUENCY, 494; ÆTIOLOGY, 496;	
SYPHILIS	461	COURSE, 498; MACROSCOPIC	
TUBERCLE	462	APPEARANCES, 500; CYTOLOGY,	
LEPROSY	467	501; STRUCTURE, 504; PIG-	
NODULAR CHOROIDITIS	467	MENTATION, 511; DEGENERATION,	
Degenerations	468	516; HÆMORRHAGE, 517; CHANGES	
SENILE CHANGES	468	IN OTHER PARTS OF THE EYE,	
ATROPHY	468	521; WITH PHTHISIS BULBI,	
VASCULAR DEGENERATION	469	524; WITH NECROSIS, 525;	
"COLLOID BODIES"	470	FLAT, DIFFUSE, OR INFILTRAT-	
OSSIFICATION	480	ING SARCOMA	529
		METASTATIC SARCOMA	533
		METASTATIC CARCINOMA	533

CHAPTER X

THE RETINA

542

The Normal Retina	542	Inflammation and De-	
ARTEFACTS	546	generation—continued.	
Wounds and Injuries	547	LIFERATIVE CHANGES, 572;	
HÆMORRHAGE, 559; LEUCOCY-		NEUROGLIA	576
TOSIS, 561; CICATRISATION	564	DEGENERATION	577
Inflammation and De-		THE RETINAL NERVOUS ELE-	
generation	567	MENTS, 578; THE NEUROGLIA,	
INFLAMMATION	568	582; OSSIFICATION, 587; THE	
VASCULAR CHANGES, 568; PRO-		VESSELS, 587; THE PIGMENT	
		EPITHELIUM	591
		SENILE DEGENERATION	596

CHAPTER X—*continued.*

THE RETINA—*continued.*

	PAGE
Special Forms of "Retinitis"	597
PURULENT, METASTATIC, AND SEPTIC RETINITIS	597
EXOGENOUS PURULENT RETINITIS, 597; ENDOGENOUS (METASTATIC) PURULENT RETINITIS, 598; RETINITIS SEPTICA (ROTH)	599
RETINITIS CIRCINATA	600
RETINITIS PIGMENTOSA	602
CHOROIDO-RETINITIS	607
RETINITIS PROLIFERANS	609
SYPHILIS	615
TUBERCLE	617
LEPROSY	621
Cysts	621
PERIPHERAL CYSTIC DEGENERATION, 621; CYSTS IN DETACHED RETINÆ	623
Tumours	626
GLIOMA	626
FREQUENCY, 626; COURSE, 627; MACROSCOPIC APPEARANCES AND GENERAL STRUCTURE, 627; CYTOLOGY, 630; DEGENERATIVE CHANGES, 633; THE VESSELS, 635; ORIGIN AND PROPAGATION, 636; CHANGES IN OTHER PARTS OF THE EYE, 639; WITH ATROPHIA BULBI, 642; WITH TEMPORARY RETROGRESSION, 644; HISTOGENESIS, 645	
OTHER PRIMARY TUMOURS OF THE RETINA	650
ANGIOMA, 651; MELANOMA	651

CHAPTER XI

THE OPTIC NERVE 652

The Normal Optic Nerve	652	Wounds and Injuries	672
THE SHEATHS, 652; THE INTRACRANIAL PORTION, 653; THE INTRA-ORBITAL PORTION, 653; THE INTRA-BULLEAR PORTION, 654; ARTEFACTS, 657; THE NEUROGLIAL MANTLE, 658; THE NORMAL VESSELS	659	Inflammation	673
Corpora Amylacea	659	PAPILLITIS	674
Hyaline Bodies (Drusen).	661	INFLAMMATION OF THE NERVE-TRUNK	676
		PERINEURITIS	680
		PACHYMEINGITIS CHRONICA	682
		METASTATIC NEURITIS	682
		SYPHILIS	683
		TUBERCLE	683
		LEPROSY	685

CHAPTER XI—*continued.*THE OPTIC NERVE—*continued.*

	PAGE
Degenerations	685
SENILE DEGENERATION	685
SECONDARY ATROPHY	686
PRIMARY ATROPHY	689
VASCULAR DEGENERATION	690
Tumours	693
PRIMARY INTRA-DURAL TU- MOURS	693
PRIMARY EXTRA-DURAL TU- MOURS	704

CHAPTER XII

THE ORBIT 716

Cysts	716	Tumours—<i>continued.</i>	
Congenital Cysts	716	NEUROMA	730
DERMOID AND TERATOID CYSTS, 716; INCLUSION CYSTS	721	PLEXIFORM NEUROMA	730
Acquired Cysts	722	SARCOMA AND ENDOTHELIOMA	738
IMPLANTATION CYSTS, 722; SER- IOUS CYSTS	722	PRIMARY SARCOMATA	738
Parasitic Cysts	723	CLASSIFICATION, 738; FRE- QUENCY, 739; CYTOLOGY, 740; PIGMENTATION, 741; STRUCTURE, 742; MYXO- SARCOMA, 744; CHONDRO- SARCOMA, 744; MYO-SAR- COMA, 745; GLIO-SARCOMA	745
HYDATID CYSTS, 723; CYSTICER- CUS CYSTS, 724; FILARIE	725	SECONDARY SARCOMATA	745
Tumours	725	OSTEOMA	745
HÆMANGIOMA	725	TUMOURS INVOLVING THE WALLS OF THE ORBIT SECONDARILY	747
LYMPHANGIOMA	727	TUMOURS OF THE FRONTAL SINUS, 747; OF THE ETH- MOID, 748; OF THE SPHEN- OID	748
LIPOMA	727		
FIBROMA	728		
LYMPHOMA	728		

CHAPTER XIII

THE LACRYMAL APPARATUS 749

The Normal Lacrymal Apparatus	749	Tumours of the Lacrymal Gland	752
Cysts of the Lacrymal Gland	751	Dacryocystitis	757
		Concretions in the Can- aliculi	758

ABBREVIATIONS

- A. d'O.—Archives d'Ophthalmologie.
- A. f. A.—Knapp and Schweigger's Archiv für Augenheilkunde. (Articles in A. f. A. are often translated or abstracted in A. of O., and *vice versa*; the reference is usually given to one only.)
- A. f. O.—v. Graefe's Archiv für Ophthalmologie.
- A. of O.—Knapp's Archives of Ophthalmology.
- B. d. o. G.—Bericht der ophthalmologische Gesellschaft zu Heidelberg. (The earlier reports are contained in K. M. f. A.)
- B. z. A.—Deutschmann's Beiträge zur Augenheilkunde. (The reference is given to the part [Heft], not to the volume.)
- C. f. A.—Hirschberg's Centralblatt für praktische Augenheilkunde.
- G.-S.—Graefe-Saemisch, Handbuch der gesamten Augenheilkunde. (The date determines the edition: 1st edition, 1874—1877; 2nd edition, 1898— .)
- K. M. f. A.—Zehender's Klinische Monatsblätter für Augenheilkunde.
- R. L. O. H. Rep.—Royal London Ophthalmic Hospital Reports.
- T. Am. O. S.—Transactions of the American Ophthalmological Society.
- T. O. S.—Transactions of the Ophthalmological Society of the United Kingdom.
- Z. f. A.—Zeitschrift für Augenheilkunde.
- *.—The most important articles are marked with an asterisk (*).

ERRATUM.

FIG. 282.—DETACHMENT OF THE VITREOUS *should read* PYRAMIDAL ANTERIOR CAPSULAR CATARACT.

CHAPTER VII

THE LENS

THE NORMAL LENS

THE lens is developed as an invagination of the superficial epiblast, so that the centre corresponds with the epithelial surface. Unlike most epithelium, the surface cells cannot be cast off, so that the centre also contains the oldest cells. These facts are of prime importance in considering the pathological changes which the lens is liable to undergo.

The epithelial cells are specially differentiated into fibres, so arranged as to subserve optical purposes. The anterior cells, covering the whole anterior surface as far as the equator, are cubical in section, polygonal when viewed on the flat (Hosch, Leber); Hosch considers that there are processes, like those in prickle-cells (Fig. 268). Surrounding the whole epithelial mass is a thin homogeneous membrane, *the lens capsule*, which is a product of secretion of the epithelium. The capsule is thickest anteriorly towards the periphery; it is thinner at the anterior pole (0.02 mm.), and much thinner at the posterior pole (0.005 mm.). This fact is in favour of the cuticular nature of the membrane (Schwalbe). The thickness increases with age, and the capsule becomes finely fibrillated. The capsule does not stain with elastic tissue stains (Weigert, Unna-Tänzer); it most nearly resembles the sarcolemma of muscle (Chittenden).

The fibres of the zonule of Zinn are inserted into the capsule at or near the equator; they are arranged in groups which may be named, according to their origin and destination, orbiculo-antero-capsular, orbiculo-postero-capsular, cilio-postero-capsular, and cilio-equatorial (Garnier) (Figs. 269 270). There is free intercommunication between the fibres, so that the canal of Petit is not a closed space, but merely represents the perilenticular space between the equator of the lens and the ciliary processes.

The posterior cells of the primitive lens vesicle elongate into fibres. Later in life the development of new fibres is limited to the anterior epithelium, which shows mitotic figures (Henle); by this means the anterior equatorial cells are continually pushed outwards and backwards, undergoing no further multiplication, but only progressive growth and development into fibres. It is unnecessary to discuss the

exact arrangement of the fibres here. It is sufficient to state that the youngest fibres are at the periphery, the oldest at the centre.

The lens fibres are long, flat bands, prismatic in section, usually hexagonal, but often irregular or rounded. They are cemented together by substance which stains faintly with ordinary stains. Each of the younger fibres contains a nucleus, which is round or elliptical; in the older fibres the nuclei show irregularities and aggregations of chromatin, which stain deeply and are frequently situated at the periphery; finally the nuclei break up and disappear in the oldest fibres. The fibres themselves become denser and less elastic with age, probably through loss of water. These old, inelastic fibres are central and form the *nucleus* of the lens, the periphery being distinguished as the *cortex*.

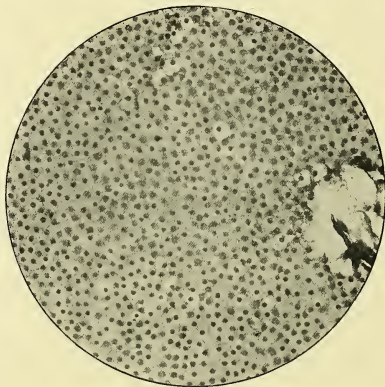


FIG. 268.—ANTERIOR EPITHELIUM OF LENS.
Removed by capsule forceps.

The sclerosis of the fibres begins in early life and increases continuously, so that the nucleus grows at the expense of the cortex; this accounts for the loss of elasticity of the lens and the consequent loss of the power of accommodation. Just as the epithelium of the skin, however, continues to grow throughout life, so the development of new lens fibres continues, though less rapidly, as time goes on. Hence the lens, unlike most other parts of the body, does not cease to grow, but continuously enlarges to the time of death (Priestley Smith). This is a fact of considerable pathological importance. Histologically, the effect of these phenomena is that the nuclei of the fibres diminish in numbers relatively, and even absolutely, as age increases.

A meridional section of the adult lens shows a small central part in which the fibres run in an axial direction, those around being convex outwards. The older fibres have a wavy or dentate contour, probably

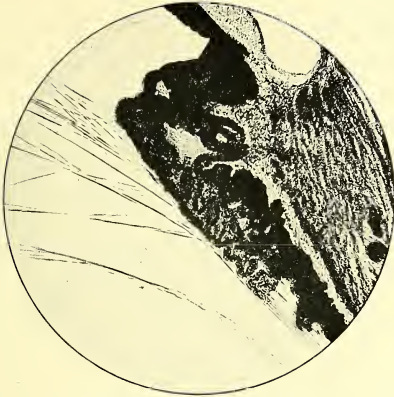


FIG. 269.—THE SUSPENSORY LIGAMENT.

Treacher Collins, R. L. O. H. Rep., xvi, 2. The orbiculo-antero-capsular fibres are seen on the pars plana of the ciliary body, and pass forwards to form the most anterior fibres. The orbiculo-postero-capsular fibres are most posterior.



FIG. 270.—THE SUSPENSORY LIGAMENT.

Treacher Collins, R. L. O. H. Rep., xvi, 2. The cilio-equatorial fibres are seen passing direct from the ciliary processes to the equator of the lens. The cilio-postero-capsular fibres cross the orbiculo-antero-capsular and the cilio-equatorial, and pass to the back of the lens.

due to shrinking. Only the peripheral fibres are arranged concentrically. According to Rabl, the lenses of all vertebrates show radial lamination in equatorial section, so that they resemble an orange rather than an onion.

Halben has examined anatomically the "apparent cataract," which, without actual opacity other than that caused by unequal refrangibility, may be the precursor of black cataract or of senile cataract.

Artefacts.—Satisfactory sections of the lens are more difficult to obtain than those of any other part of the eye. This is partly due to its hardness, and particularly to the inequality of hardness of different parts, and partly to the difficulty of avoiding artefacts. The usual hardening reagents—alcohol, formol, chromate solutions, etc.—give very inaccurate results. As pointed out by E. v. Hippel, formol causes considerable shrinking, especially if the globe is not opened. It is indeed very difficult, and may be impossible, to determine whether a lens is cataractous after hardening in the usual manner with formol, at any rate, before sections are examined microscopically. If formol is used, it should not be stronger than 5 per cent.; Rabl used sublimate platinum chloride and sublimate picric acid mixtures. Treacher Collins recommends Müller's fluid. Halben recommends Rabl's sublimate picric acid mixture, formol (2—4 per cent.), or formol and alcohol.

In sections the capsule is often broken, especially in the thinnest part. Fluid is frequently pressed out of the cells and fibres, which apparently have no membranous envelope, into the lymph spaces between the fibres. Homogeneous or granular deposits are thus produced which cannot be distinguished from cataractous deposits. In lenses obtained *post mortem* there may even be true Morgagnian globules lying under the anterior cells or posterior capsule. Spindle-shaped spaces between the fibres are common; round spaces, when they contain deposits, are never artefacts. The lens may shrink away from the capsule, which is then thrown into folds.

HENLE.—Göttinger Nachrichten, 1875; Abhandl. d. k. Gesellschaft d. Wiss. zu Göttingen, 1878. CHITTENDEN.—Untersuchungen d. phys. Institut zu Heidelberg, 1879. BERGER.—A. f. O., xxviii, 2, 1882; xxxi, 3, 1885. *O. BECKER.—Zur Anat. der gesunden u. kranken Linse, Wiesbaden, 1883. PRIESTLEY SMITH.—Brit. Med. J., 1883; Glaucoma, London, 1891. SCHWALBE.—Anat. des Sinnesorgane, Erlangen, 1887. GARNIER.—A. f. A., xxiv, 1891. TOPOLANSKI.—A. f. O., xxxvii, 1, 1891; K. M. f. A., xxxii, 1892. E. v. HIPPEL.—A. f. O., xlv, 2, 1898. *RABL.—Ueber den Bau u. die Entwicklung der Linse, Leipzig, 1900. SCHULTZE.—In G.-S., 1900 (Bibliography). HOSCH, LEBER.—A. f. O., lii, 3, 1901. HALBEN.—A. f. O., lvii, 2, 1903.

CATARACT IN GENERAL.

All the changes which occur in the lens are essentially degenerative. As in the case of the vitreous, there are no blood-vessels; further, there is no mesoblastic tissue, so that inflammation—so-called "phakitis" (Iwanoff)—is impossible. Secondary changes occur as the result of inflammation in surrounding structures: these are also chiefly degenerative, the only active response to irritation being a lowly type of proliferation of the cells of the anterior capsule (*v. infra*).

The lens fibres.—The lens fibres themselves may appear but little altered in spite of other evidence of cataract. The earliest change, in



FIG. 271.—“DOTTED” CATARACT.

From a photograph by Mayou. The opacities are caused by albuminous deposits in spindle-shaped spaces between the lens fibres. The coagulated deposits stain deeply with hæmatoxylin.

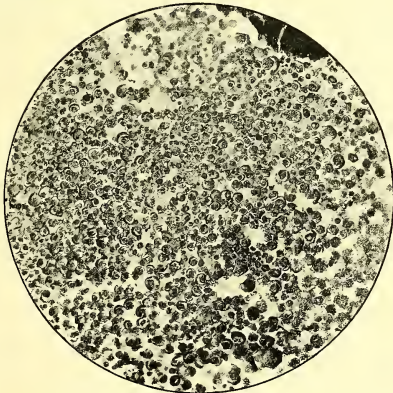


FIG. 272.—TRAUMATIC CATARACT. $\times 100$.

Morgagnian globules, broken-down lens fibres, granular *débris*, etc., undergoing absorption.

fact, consists in the separation of the fibres from each other, owing to over-shrinking of the nucleus ; fissures are thus produced, which are

filled with liquid (*cf.* Fig. 271). They are first formed where the nutrition of the lens is best, viz. at the equator (Figs. 206 and 207, vol. i). The liquid coagulates into drops or spheroidal bodies, the Morgagnian globules (Figs. 272, 273, etc.).

It has already been pointed out that the lens fibres normally undergo sclerotic changes, resulting in the formation of the lens nucleus. The thickness of the fibres then varies, and their contours become wavy or dentate. The same changes may happen in the cortical fibres under pathological conditions. The earliest change is usually swelling, though this may be preceded by a granular cloudiness, due to fatty degeneration. Some fibres become spindle-shaped, others club-shaped, others assume grotesque forms. Round globules may be

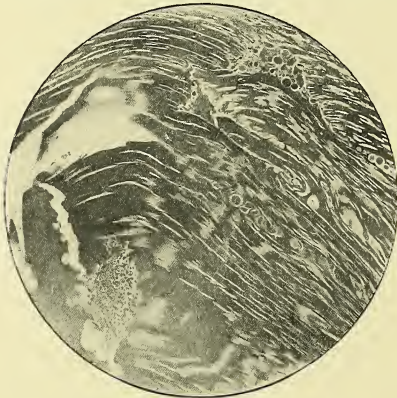


FIG. 273.—CATARACTOUS LENS. $\times 55$.
From a shrinking globe.

seen, and if these contain a nucleus they much resemble the vesicular cells (*v. infra*). Vacuoles are seen, which run together and form cystic spaces, filled with fluid (Figs. 136, 182, and 223, vol. i). Finally, the fibres break up into globules, much resembling the Morgagnian globules; they are sometimes badly termed "myelin" droplets (Fig. 273). These are round bodies, which stain faintly with eosin, etc.; they are often polygonal through mutual pressure. When they lie in rows in a space, the latter often shows a double contour, so that the whole resembles a row of vegetable cells, such as are seen in algæ. The Morgagnian globules do not stain with hæmatoxylin, and they are very resistant to reagents.

Just as the nuclei degenerate under normal circumstances in the formation of the lens nucleus, so they undergo similar changes pathologically. They become long and narrow, and vacuoles appear, often

forming a clear zone around them. The chromatin becomes arranged into transverse bands, granules, etc., which stain very deeply with nuclear stains. When the nucleus is no longer to be seen, a clear spot frequently marks its former site for a considerable period.

In more advanced cases globules which stain deeply with hæmatoxylin may be found. These are of two kinds: some do not dissolve in mineral acids, so that they resemble hyaline deposits elsewhere. Others dissolve under these conditions, giving off gas, and showing other reactions which demonstrate their calcareous nature.

In the later stages, too, the fissures and spaces increase in size and vary in shape. They contain various substances: clear fluid, albuminous coagula, *débris*, Morgagnian globules, droplets of fat, fatty crystals,



FIG. 274.—DISLOCATED LENS. $\times 55$.

Lens dislocated upwards and forwards; from a man, æt. 61. Capsule intact. Note iris pigment on capsule, and disappearance of anterior cubical epithelium.

cholesterin (Lang, Gunn), crystalline deposits (Axenfeld and Krukenberg, Baas, Besserer, Stock), etc. Albuminous coagula may resemble in every respect the globules formed by the breaking up of lens fibres; or they may appear as granular coagula, such as are found in other parts. The granules may be large, or they may be so small that the masses look homogeneous until they are examined with very high powers. Concentric lamination is rare. These coagula resemble Morgagnian globules in their resistance to reagents, but differ from them in staining deeply with hæmatoxylin. Carmin stains them yellowish brown, benzoazurin blue (Heinzel), carbol fuchsin and iodine green (Russell's stain) deep blue; Weigert's elastic tissue stain does not stain them. The staining is often diffuse and irregular.

In some degenerated lenses peculiar coiled-up fibres are seen, stain-

ing deeply red with van Gieson (Werncke). Fibrin-like masses have also been observed (Zia).

The epithelium.—The epithelium is the only part of the lens which shows definite signs of proliferative reaction. The degenerative changes may, however, be described first. These are normal to old age, when the cubical cells become flatter, and at the equator show processes. The nuclei show fewer mitoses and are diminished in numbers, though those that remain stain more deeply than usual.

The epithelium may be destroyed entirely, as in a case of glaucoma recorded by E. v. Hippel, and also in two eyes containing foreign bodies. v. Hippel regards the disappearance of the epithelium as useful, since it allows the aqueous to pass through the capsule, thus aiding the absorption of the lens matter. The cells also become absorbed, after previous vacuolisation, in cataract following lightning stroke (Kiribuchi).

Vacuolisation has been most minutely studied by Schirmer in the lenses of rabbits after massage by Förster's method. The cytoplasm showed the first changes, becoming finely granular and ultimately breaking down. In the nuclei vacuoles appeared, breaking up the chromatin into globules, *débris*, and fibrils. The fluid accumulates around the remnants of the chromatin, forming a clear zone. The smallest and most deeply stained nuclei contain the smallest vacuoles and the broadest zone, whilst in the intermediate stage the nucleus may be sickle-shaped. These changes, dependent upon massage, are not due to direct destruction by pressure, but the cells are probably so injured that they cease to cause any impediment to the filtration of the aqueous; hence the vacuolisation. The changes commence about half an hour after trituration.

Degeneration of the epithelium may be preceded by signs of irritation, as shown by increased deposition of capsular material. In this manner hyaline nodules (Drusen), similar to those found on other hyaline membranes, may be formed on the inner surface of the capsule. They are commonest in over-ripe cataracts (Becker), and were attributed by H. Müller to degeneration of the nuclei (*cf.* "Colloid Bodies" of the Choroid).

Proliferative changes in the anterior capsular epithelium are seen *par excellence* in anterior capsular cataract (q. v.). They have been studied experimentally by Schirmer as they occur in late stages after trituration of the lens. They are also found occasionally in other pathological conditions, *e. g.* covering the posterior surface of hyaline bodies on the inner side of the capsule (Becker).

Proliferation of the epithelium may cause the cells to extend beyond their normal termination at the equator, so that the whole of the posterior capsule may become lined (Becker). This may occur very rapidly after the interference with the normal whorl-like arrangement of fibres at the equator; it prevents the formation of new fibres, since the new cells do not elongate in the usual manner. They are not regular, however, like the anterior capsular cells, but vary in size and shape. Masses of such cells were found by van Geuns after tying vortex veins in rabbits. Treacher Collins attributes the growth of epithelial cells beyond the equator to diminished tension of the capsule, produced by



FIG. 275.—SENILE CATARACT.

Treacher Collins, T. O. S., x. Senile cataract with peculiar distribution of the degenerative changes, and complete lining of the posterior capsule with epithelium.

the degeneration and shrinkage of the cataractous lens fibres (Fig. 275). The fibres near the equator, in the nucleated zone, are often found broken up in these cases.

More common is the formation of vesicular cells (Blasenzellen, Bläschenzellen [Wedl]). These, as already stated, may be formed from lens fibres, but they originate for the most part in epithelial cells. Thus they may be found anteriorly when the cubical cells have been separated from the capsule, or more often in new cells lining the posterior capsule. According to Becker they are due to "hydropic" degeneration of the cells; this is not the true explanation, which is rather to be sought in the inherent tendency of the cells to produce fibres. The cells are large and swollen, spherical or polygonal from pressure; they contain each a faintly staining nucleus, which later degenerates and disappears, though its former site may be recognisable as a clearer spot. The nuclei never show mitotic figures, nor have these been seen in cells lining the posterior capsule in man, though they have been observed in rabbits (van Geuns).

FOERSTER.—A. f. O., iii, 2, 1857. H. MÜLLER.—Gesammelte Schriften, Leipzig, 1872. *O. BECKER.—Zur Anat. der gesunden u. kranken Linse, Wiesbaden, 1883. SCHIRMER.—A. f. O., xxxiv, 1, 1888; xxxv, 1, 1889. WAGENMANN.—A. f. O., xxxv, 1, 1889. LANG, MARCUS GUNN, T. O. S., xv, 1895. TREACHER COLLINS.—T.O.S., x, 1890; Researches, London, 1896.—MEYER.—A. f. O., xlv, 3, 1898. VAN GEUNS, A. f. O., xlvii, 2, 1899. KIRIBUCHI.—A. f. O., l, 1, 1900. AXENFELD AND KRUKENBERG.—B. d. o. G., 1900. BAAS.—A. f. O., xlv, 3, 1897. BESSERER.—Dissertation, Freiburg, 1899. STOCK.—K. M. f. A., xl, 1902. WERNCKE, K. M. f. A., xli, 1903, Beilageheft. ZIA.—Z. f. A., xii, 1904.

SPECIAL FORMS OF CATARACT

SENILE CATARACT

The changes in senile cataract are confined to the cortex at first; the epithelium and nucleus suffer only slightly in the later stages.

In incipient cataract spaces are found between intact fibres, especially in the equatorial region; they contain clear fluid, or coagula and Morgagnian globules. Becker attributes the condition to excess of the physiological shrinking of the nucleus, and Priestley Smith points out that these lenses are smaller than normal. According to Alt, more fluid passes in from without, but this is improbable in the early stages owing to the protective influence of the epithelium. The radial wedge-shaped areas of opacity (Fig. 276) may be due to the arrangement of the lens star (Alt), but this is doubtful, since there are often more than nine, the highest number of rays yet found in the lens star. Nevertheless, it is caused by the radial lamination, the spaces fusing by the breaking down of the intervening lamellæ. The microscopical appearances are, then, those which have already been described—club-shaped and spindle-shaped fibres, vesicular cells, coagula, Morgagnian globules, etc.



FIG. 276.—SENILE CATARACT.

After Lawson. A. Front view. B. Sectional view.

The epithelium may be quite normal (Ginsberg), but the early destruction of the equatorial fibres removes the obstruction to proliferation in this direction, so that the cells often extend towards the posterior pole, and even line the posterior capsule (Treacher Collins) (*v.* p. 396). The excessive shrinking of the nucleus also relieves pressure, and increases the supply of nutriment (Becker). Hence the anterior epithelium also proliferates, forming two or more rows, often containing vesicular cells. The proliferation is usually general, but may be circumscribed.

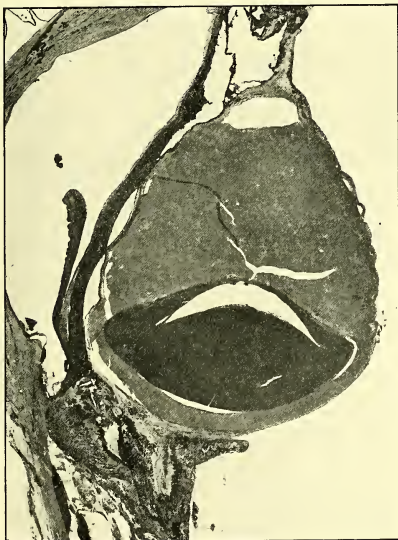


FIG. 277.—MORGAGNIAN CATARACT. $\times 10$.

From a specimen by Treacher Collins. The capsule contains albuminous fluid which has stained; the nucleus (dark) has sunk to the lowest part, and lies with the long axis antero-posterior.

The spaces between the fibres, filled with coagula which are deeply stained with hæmatoxylin, increase in numbers, and more and more fibres break up, with the formation of large irregular spaces, until finally the whole cortex is transformed into a cataractous mass. All the constituents already mentioned, including cholesterin and even calcareous material, are found. Some of the lens substance is absorbed, so that the contents shrink away from the capsule, which thus becomes separated by a thin layer of fluid. The cataract is then said to be *ripe*.

The proliferation of epithelium may lead to the formation of a definite anterior capsular cataract, most resembling the inflammatory type (*v. infra*). This condition is apparently constant in *hypermature* cataracts, and accounts to some extent for the thickening of the capsule. In these cases the lens substance is gradually absorbed and partially replaced by fluid, in which the nucleus lies free—*Morgagnian cataract* (Fig. 277). Even in these late stages the nucleus remains unaltered, or at most shows an eroded surface, due to slight absorption (Becker).

*BECKER.—Zur Anat. der gesunden u. Kranken Linse, Wiesbaden, 1883. SCHOEN.—A. f. A., xvii, 1887; xix, 1889. TREACHER COLLINS.—T. O. S., x, 1890. ALT.—Amer. Jl. of Ophth., 1899. E. v. HIPPEL.—A. f. O., l, 3, 1900. *RÖMER.—A. f. O., lx, 2, 1905.

Cataracta senilis præmatura punctata (Becker), or "punctate" cataract, commences at 30—40 years of age; it has been examined microscopically by Hess. Here, again, the nucleus is normal, and the perinuclear fibres are also normal, though separated by spaces containing homogeneous or finely granular masses. The spaces are spindle-shaped, and may be filled with the coagula, though the latter are more commonly elliptical. The spaces may also be elliptical, probably according to the direction in which they are cut. They are most numerous outside the equator of the nucleus, and do not communicate with each other. The coagula stain deeply with hæmatoxylin, brownish yellow with ammonia carmin; they swell up somewhat with hydrochloric, nitric, and acetic acids. In Becker's case the fibres showed a wavy contour, and there were groups of vesicular cells under the anterior capsule.

BECKER.—Zur Anat. der gesunden u. Kranken, Linse, Wiesbaden, 1883. HESS, A. f. O., xxxix, 1, 1893.

Cataracta nigra.—Black cataracts are due to complete sclerosis of the lens, *i. e.* the whole of the lens becomes transformed into nucleus. The fibres lose their dentations and become fused into an almost homogeneous mass, the nuclei diminish in numbers, and no new fibres are formed. The epithelial cells become flattened, and the nuclei stain less deeply; the capsule becomes thickened. It is probable that the so-called "apparent cataract" is the early stage of black cataract (Halben). The completely developed black cataract is rare; it is said to occur most in myopic eyes. The colour is a dark mahogany brown, and shows on chemical and spectroscopic tests no signs of blood-pigments; it is probably merely an exaggeration of the normal amber colour.

A very black variety has been described by McHardy; it was examined spectroscopically by McMunn, who found no trace of hæmoglobin, methæmoglobin, or hæmatin. He considered that the pigment belonged to the class of melanins.

Very dark lenses may be found in cases of hæmorrhage (*v. Graefe*, Gillet de Grandmont, Moauro). Here chemical and spectroscopic examination reveal the presence of blood-pigments. Linde found experimentally in rabbits that blackish brown crystals formed in the fibrin on the capsule and the cortex became stained reddish-brown, the nucleus remaining free.

EDWARDS.—Dissertation, Paris, 1814. BECKER.—Zur Anat. der gesunden u. Kranken Linse, Wiesbaden, 1883. MCHARDY.—T. O. S., ii, 1882. V. GRAEFE.—A. f. O., i, 1, 1854.

POWER.—T. O. S., v, 1885. GILLET DE GRANDMONT.—A. d'O., xiii, 1893. LINDE.—C. f. A., xx, 1896. MOAURO.—Riforma med., 1896. ALT.—Amer. Jl. of O., xvii, 1900. HALBEN.—A. f. O., lvii, 2, 1903.

LAMELLAR CATARACT AND ALLIED FORMS.

Lamellar, zonular, or perinuclear cataract has been frequently examined microscopically: Deutschmann (1886), Beselin (1887), Lawford (1888), Schirmer (1889), Dub (1891), Peters (1893), Hess (1893), E. v. Hippel (1895), Treacher Collins (1896), Bach (1897), Heinzel (1899). Hulke states that the condition was first demonstrated macroscopically by Bowman in 1846 on the lens of a kitten.

Deutschmann made the first microscopical examination. He found the nucleus and cortex normal, but separated by a zone in which the lens fibres were altered by the presence of numerous vacuoles and droplets of "myelin"; there were also fissures between the fibres filled with granular *débris*.

Beselin found scattered throughout the nucleus small masses, which he attributed to *post-mortem* coagulation products. The nucleus was surrounded by two oval zones of cataractous substance, incomplete and discontinuous, separated by a layer of normal lens tissue.

Lawford examined three lenses; the line of demarcation between the cortex and nucleus was abrupt, and contained a thin layer of granular substance, probably constituting the essential part of the zonular cataract (Figs. 280, 281). In the nuclear area of all three specimens were numerous small irregular dots, arranged more or less in layers running concentrically. These he attributed to artefacts.

Schirmer, examining six cases, found a similar vacuolated condition of the nucleus, the vacuoles being more numerous in what he regards as the zone of opacity than in the central portion. He proved subsequently that the vacuoles were present in a fresh lens, and that they correspond with the opaque zone seen before and after extraction. The clefts described by Beselin and Lawford are probably the riders so often seen in lamellar cataracts. Double and triple zones have often been observed clinically. Schirmer examined a case of the latter condition.

Hess examined five cases, and confirmed Schirmer's results.

Treacher Collins examined seven cases. He found three kinds of changes; they were not all present in each lens, and the amount of change varied considerably. First, there are fissures between the lens fibres, which may or may not contain a granular substance; they run concentrically to the nucleus, separating it from the cortex. Secondly, small vacuoles are found, mostly round or oval, but in places elongated and beaded; some contain a hyaline substance which after prolonged immersion in hæmatoxylin stains deeper than the surrounding fibres. The average size of the vacuoles is about 5μ in diameter. Thirdly, there



FIG. 278.—LAMELLAR CATARACT.

After Lawson. A. Front view. B. Sectional view.

are spaces larger than the so-called vacuoles, measuring on an average 20μ across, mostly circular, with very irregular margins, and containing a granular substance which stains deeply with hæmatoxylin; apparently some degeneration of lens substance occurred in their formation. These three changes correspond with the appearances seen clinically, viz. the radiating spokes or riders, the uniform haze, and the denser dots.

Subsequent observers have found the same appearances, which they have examined in further detail. The contents of the vacuoles, which diminish in number from without inwards, generally stain with hæmatoxylin and benzoazurin (Heinzel); sometimes they do not stain, thus resembling the albuminous deposits in senile cataract. Ginsberg found them unstained by hæmatoxylin and Russell's stain, but coloured pink with Weigert's resorcin-fuchsin stain; sometimes the walls of the spaces stain when the contents remain colourless. The large sickle-shaped

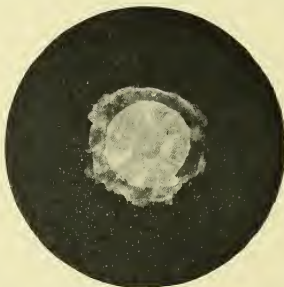


FIG. 279.—LAMELLAR CATARACT.

The lens was extracted and photographed in water. The clear peripheral cortex is seen adhering to the cataractous part.

clefts corresponding to the riders and their contents give the same staining reactions as the vacuoles.

The nucleus is often shrunken and distorted; it may be biscuit-shaped, the cortical fibres filling the concavities (E. v. Hippel). The nucleus is sometimes adherent to the posterior (Schirmer, Hess) or even the anterior capsule. Heinzel has described such a case. This is probably the cause of *fusiform* or *axial cataract* (Knies, Leber); the points of adhesion naturally remain free from the later superposed cortical fibres, so that the nucleus becomes pulled out antero-posteriorly. All the axial cataracts hitherto observed have been combined with a zonular or a central cataract (Bach). It has been thought by some that axial cataract is due to disturbance of the nutrition of the lens in early foetal life, while the fibres run in an axial direction. Hess, from examination of the chicken embryo, is of the opinion that it is caused by delayed union of the mouth of the lenticular sac, and that all the fibres present at this date become more or less opaque, especially the strands running from the nucleus to the point where the sac has finally closed. Bach

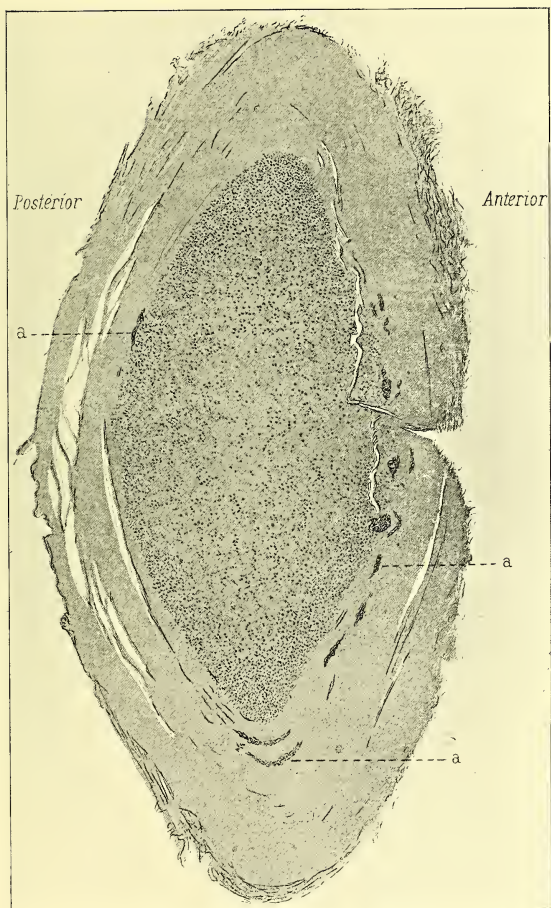


FIG. 280.—LAMELLAR CATARACT. $\times 25$.

Lawford, R. L. O. H. Rep., xii. *a, a, a*. Fragments of the rope-like line separating the central and cortical parts; this is double in places, *e. g.* below. Note the opacities in the nucleus.

has described an axial cataract from a rabbit. The opaque band ran from an anterior capsular cataract to a thicker part in the nucleus, and was continued to the posterior pole by a thread, which then again broadened out. The opaque band consisted of degenerated lens fibres with fine black pigment in places, and many small vacuoles and coagula at the sides.

Central or nuclear cataract shows exactly the same changes that are found in lamellar, but the vacuoles are more numerous (Schirmer).



FIG. 281.—LAMELLAR CATARACT. $\times 85$.

Lawford, R. L. O. H. Rep., xii. Anterior surface above. Note boundary between nucleus and cortex, and globules in former.

The same changes were also found in the nucleus in a case of *total congenital cataract* examined by Hess. The condition occurred in a child of six months, and was bilateral; the right lens was needled, after which the child died of pneumonia. The whole of the cortex was homogeneous except a few normal fibres at the equator. The nucleus contained vacuoles of various sizes at the periphery, marking it off sharply from the cortex; the central part was composed of concentric fibres, with large and small drops (0.023—0.024 mm. in diameter), staining deeply with hæmatoxylin. The fluidity of the outer cortical parts was attributed to rickets; the vitreous was normal.

Varicous theories have been advanced to account for lamellar cataract; the question cannot be said to be definitely settled. Horner considered that a pathological layer of lens fibres was deposited about a normal nucleus, the cause being rickets, which also accounted for the changes in the enamel of the teeth which so frequently accompany the disease, as well as the convulsions, which were due to the associated craniotabes. This view has been widely accepted on the Continent. Leber considered that a normally formed layer of fibres became subsequently changed. Beselin asserted that alterations in the nutrition affect the whole nucleus, which, at the time when they occur, represents the whole lens; the general contraction of the affected part causes the formation of fissures between it and the cortical layers of normally formed lens substance which are developed later.

Schirmer considers that some unknown disturbance, probably of nutrition, affects the lens so as to produce vacuoles in its substance. These may be at first in the fibres, but are certainly found later between them. The later formed fibres are normal and transparent. According to the time and the intensity of the injurious action the different forms of cataract arise, central cataract by very early and intense malnutrition, lamellar cataract by later and moderate injury. Hess adds the congenital total cataract as an example of still more prolonged malnutrition, whereby even the later deposited cortical layers also suffer.

There has been much discussion as to whether lamellar cataract is congenital or infantile. The decision turns largely upon the size of the opaque area as compared with the size of the lens at birth. Dub has used an ingenious optical method for measuring the diameter of the opacity; he then compares the results with the diameter of the foetal lens as measured by Treacher Collins. He concludes that the commonly received views, that zonular cataracts begin in the first two years or so of extra-uterine life, and that the peripheral fibres are the parts affected, cannot both be true.

A number of direct measurements have now been made; some of these have been collected by Treacher Collins and compared with Dub's:

		6 mm.		Dub (1)	4.4 mm.
Beselin					
Lawford	(1)	5.25 "		" (2)	4.6 "
"	(2)	4.5 "		" (3)	4.7 "
"	(3)	4.5 "		" (4)	4.8 "
Schirmer	(1)	5.75 "		" (5)	4.8 "
"	(2)	3.25 "		" (6)	5.0 "
"	(3)	6.0 "		" (7)	5.2 "
Collins	(1)	3.5 "		" (8)	5.2 "
"	(2)	3.5 "		" (9)	5.5 "
"	(3)	5.5 "		" (10)	5.6 "

Treacher Collins found the average diameter of three lenses at the ninth month of foetal life to be 5.75 mm, and Dub found the average of three lenses under one year old to be 7.46 mm. Hence it would appear that the zone of opacity in zonular cataract is probably never larger

than the lens at birth, that it may be about the same size, but that it is generally smaller, and sometimes very much smaller.

The direct measurements differ slightly from Dub's, and show a greater variety, in three the zone being larger than his largest, and in three smaller than his smallest. In the smallest there is so much difference between the size of the zone and that of the lens at birth that it is scarcely possible to believe that the opaque area was the extreme cortex at the time of birth, and that the diminution in size is the result of shrinking (Collins). One must therefore conclude that lamellar cataract may be produced before birth, or that the part primarily affected is not the most peripheral.

Treacher Collins agrees with Beselin, Schirmer, Peters, and others that shrinking of the nucleus may occur. He thinks that it is conceivable that as the result of some general disturbance of nutrition the lens might become affected after birth, so that the nucleus, which is farthest removed from the nutrient supply, would shrink. It will be observed that this is an extension and modification of the original theory. He adduces in favour of the view the cases in which lamellar cataract has been known to arise as the result of what may be termed purely intra-ocular causes. Thus, v. Graefe described one caused by iritis with synechiæ, Becker one following a perforating ulcer of the cornea. Schirmer reported a case of anterior staphyloma, in which the lens had an anterior capsular, or an anterior polar (cortical), and a zonular cataract; Collins adds a similar observation.

There seems to be no evidence of any connection between zonular cataract and congenital syphilis. The defective condition of the enamel of the teeth so frequently associated with the former is, as Hutchinson pointed out, quite different from the notched screwdriver condition found in the latter disease. Hutchinson does not agree with Horner in attributing zonular cataract and the defect of the enamel to rickets; he considers the latter more probably due to stomatitis from the administration of mercurial powders given for fits. He considers the suggestion of the Zürich investigators, that the peculiarities of the teeth, the skull bones, and the general development are all due to rickets, wholly unproved. He was the first to point out in this connection that the so-called "rachitic teeth" refer to the permanent dentition, whereas the disease disappears before the second dentition commences. At the same time, it will be generally admitted that Hutchinson's theory is inadmissible.

Though it is not proved that rickets affects the permanent teeth, it is quite possible that it may do so. The germs of all the enamel organs of the permanent teeth are present at birth, and exactly those teeth most frequently affected—the first molars, the incisors, and the canines—are the ones in which calcification commences during the first two years of life, *i. e.* at the time of the initiatory stage of rickets.

Treacher Collins has collected some useful evidence as to the geographical distribution of rickets and lamellar cataract. In Adelaide and Melbourne both are rare; in Sydney rickets is as common as in England, lamellar cataract is less frequent. In Persia both diseases are very rare.

A very valuable contribution from the dental point of view has been recently brought forward by Bennett. The condition generally present in the permanent teeth associated with lamellar cataract is a honey-comb condition, or hypoplasia (Grevers); it is due to imperfect calcification. It is not found in the usual types of undoubted congenital cataract. Any cause tending to inhibit calcification during the first three years of life might be expected to show its effects on some part of the crowns of the first permanent molars, and on the synchronously calcified parts of the incisors, cuspids, and bicuspid. The only parts of the temporary teeth likely to be affected would be the cuspids and molars in the region of the gum margin. From observations on 26 cases of lamellar cataract Bennett concludes that the conditions found in the molars, incisors, and cuspids suggest interference with calcification from very shortly after birth up to two years of age or less. There was a history of rickets in 3 cases only, whilst 13 had convulsions in infancy. Bennett does not consider that rickets accounts for the condition, but that it is more probably due to some general derangement of health, especially those caused by errors of feeding and nutrition, possibly also acute exanthemata.

KNIES.—A. f. O., xxiii, 1, 1877. LEBER.—A. f. O., xxvi, 1, 1880. HULKE.—T. O. S., vii, 1887. DEUTSCHMANN, A. f. O., xxxii, 2, 1886. BESELIN.—A. f. A., xviii, 1887. LAWFORD.—R. L. O. H. Rep., xii, 1888. SCHIRMER.—A. f. O., xxxv, 3, 1889; xxxvi, 1, 1890; xxxvii, 4, 1891. DUB.—A. f. O., xxxvii, 4, 1891. PETERS.—A. f. O., xxxix, 1, 1893; K. M. f. A., xlii, 1904. HESS.—A. f. O., xxxix, 1, 1893; xlii, 3, 1896; xlvii, 2, 1899. *TREACHER COLLINS.—T. O. S., xv, 1895; Researches, London, 1896. E. v. HIPPEL.—A. f. O., xli, 3, 1895; liv, 1, 1902. BACH.—A. f. O., xliii, 3, 1897; xlv, 1, 1898. HEINZEL.—A. f. O., xlviii, 3, 1899. ALT.—Amer. J. of O., xvii, 1900. BENNETT.—T. O. S., xxi, 1901. STOCK.—K. M. f. A., xl, 1902.

ANTERIOR POLAR CATARACTS

Anterior polar cataracts are either capsular or cortical, the former being most common, so that it is usually designated simply "anterior polar cataract." Pathologically the conditions are quite dissimilar, though they may occur together; it is best, therefore, to distinguish carefully between the two forms. Opacities on the surface of the lens, caused by persistent vascular sheath of the lens or persistent pupillary membrane, etc., are often wrongly termed anterior polar cataract, just as the usual variety of so-called posterior polar cataract is due to a similar cause. The term "cataract" should naturally be restricted to opacities of the lens itself. *Anterior cortical cataract* occurs rarely combined with anterior capsular (q. v.); it is more common in complicated cataract (q. v.).

ANTERIOR CAPSULAR CATARACT

Anterior capsular cataract is due to a localised proliferation of the anterior cubical cells, usually accompanied by some disturbance and breaking up of the lens fibres in the neighbourhood (Fig. 102, vol. i). The development of the condition was observed and recorded by Arlt

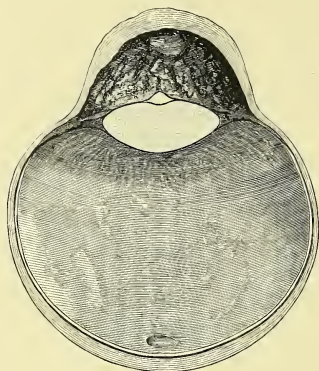


FIG. 282.—DETACHMENT OF THE VITREOUS.

R. L. O. H. Museum. From a child, æt. 7; perforating ulcer after measles. Anterior staphyloma and pyramidal anterior capsular cataract.

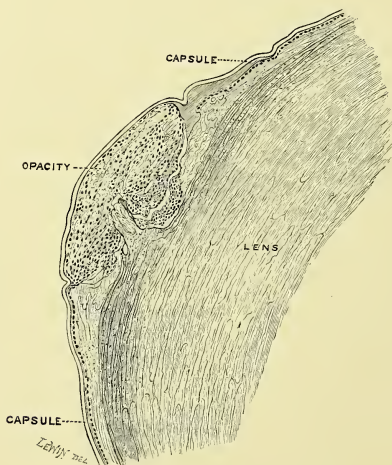


FIG. 283.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xii. An anterior capsular cataract of less than six weeks' formation. The changes are entirely beneath the hyaline capsule.

and examined microscopically by H. Müller (1856), Knies (1880), and Becker (1883). Treacher Collins has well described this form of cataract, and has added important details as to its occurrence and origin.

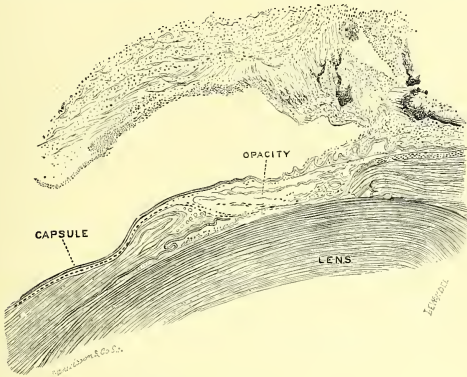


FIG. 284.—ANTERIOR CAPSULAR CATARACT.

Treacher COLLINS, T. O. S., xii. An anterior capsular cataract of less than eight weeks' formation. Note the cataract beneath the wrinkled capsule, and the inflammatory products in the pupillary area.

As a consequence of the proliferation of the capsule cells elevation of the hyaline capsule over them is brought about, and from the breaking up of the lens fibres some excavation of the lens substance beneath



FIG. 285.—ANTERIOR CAPSULAR CATARACT. $\times 55$.

From the same eye as Fig. 190, vol. i. There is a delicate vascular pupillary membrane of inflammatory origin. Note the elongated nuclei in the cataract, resembling those of connective tissue.

them occurs. Later, the mass of cells and *débris* of the broken-up lens fibres become condensed into an almost structureless substance, showing slight lamination, and having a few flattened epithelial cells scattered

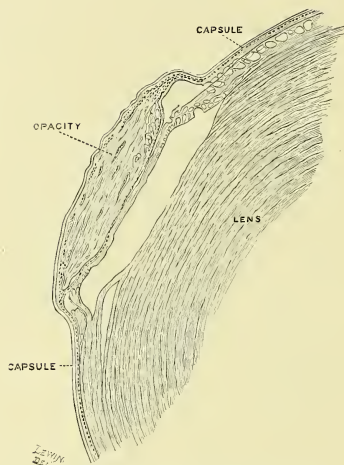


FIG. 286.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xii. An anterior capsular cataract of seven months formation. A layer of cells is shown beneath the opacity, continuous with those lining the capsule elsewhere, and in front of this is a hyaline layer.



FIG. 287.—ANTERIOR CAPSULAR CATARACT. $\times 120$.
Showing ingrowth of cubical epithelium beneath the cataract.

within it. The mass is formed by the division of the cubical cells and the extension of their protoplasm into long hyaline processes. In flat preparations the processes are seen to communicate, forming a network, in the meshes of which less altered cells are found. In vertical sections the cells are spindle-shaped, and much resemble new-formed connective-tissue cells. When isolated by teasing, they are seen to be band-like, the processes ending in sharp points (Schirmer). The cells are cemented together by a hyaline material, the whole being laminated. Chemically the mass resembles the hyaline capsule, differing, therefore, essentially from connective tissue (Schirmer). Wagenmann found cells and groups of cells surrounded by a hyaline zone of exactly the same nature as the capsule. Fragments of the cortex may be embedded in the cataract (Krüger).

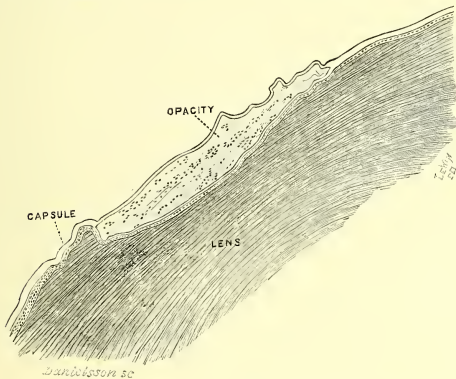


FIG. 288.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xii. An anterior capsular cataract of eleven years' formation. A complete hyaline membrane, lined by cells, is shown behind the opacity, and the lens capsule in front of it.

In the later stages the nuclei of many of the cells degenerate and disappear, so that the mass becomes still more hyaline in character. The proliferating cells seem to insinuate themselves between the neighbouring cells and the capsule; Schirmer, however, considers that this does not occur, but that small prominences are formed which invade and displace the normal cells.

After the cataract has been developed for some time there is usually, but not always, a single layer of well-formed cubical cells covering the posterior surface and separating it from the rest of the lens. It gives the appearance of the normal cells having spread in from the periphery. According to Treacher Collins this is always found after the cataract has existed for more than seven months. Later still, after several years, a layer of hyaline membrane exactly like

the capsule is found on the anterior surface of this layer of cells. The appearance is then that of splitting of the anterior capsule at the edge of the cataract, and Becker attributed the condition to this cause. It is more probable that it is analogous to the appearance of splitting of Descemet's membrane in the new-formed hyaline membranes which are seen on the surface of the iris (*see* Vol. I, p. 304): that is, the new membrane is a cuticular deposit from the new well-formed layer of epithelial cells, which continue their normal function of laying down capsule (Schirmer, Wagenmann, Gepner, Treacher Collins). According to Schirmer there is a fine line separating the old thicker normal capsule from the new thinner hyaline membrane at the periphery of the cataract. Moreover in wounds of the anterior capsule the gap is first closed by rows of cells resulting from proliferation of the capsular

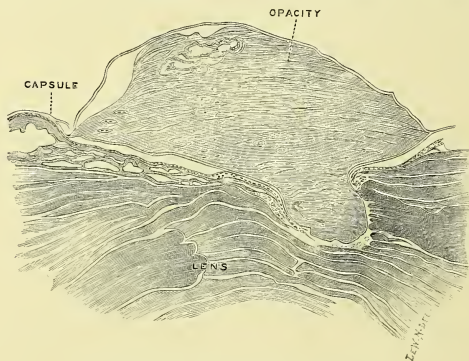


FIG. 289.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xii. An anterior capsular cataract of twenty-one years' formation. A hyaline membrane, lined by cells, is shown behind the opacity; it is equal in thickness to the lens capsule in front of the opacity.

epithelium beneath a layer of fibrin; afterwards a new hyaline layer makes its appearance, bridging over the space left by the retraction of the two extremities of the broken capsule. This new layer is evidently the product of the epithelial cells on its inner surface. Treacher Collins also found that in all the most recent anterior capsular cataracts there was no distinct layer separating the opaque part from the lens fibres (Fig. 283). In those of longer duration a layer of cells is observed between them (Figs. 286-290). In two lenses in which several years had elapsed after the formation of the cataract there was a layer of hyaline material in front of the layer of cells; it was thicker in one of twenty one years' than in one of eleven years' duration (Figs. 288, 289). Further, in one case the hyaline layer formed a complete capsule on the posterior side of the cataract.

It is sometimes observed that when there is an opacity at the

anterior pole of the lens there is also a second (cortical) opacity a short distance behind, separated from the anterior one by some clear lens matter. Treacher Collins records seven such cases; in all of them several years had elapsed between the inflammatory attack which

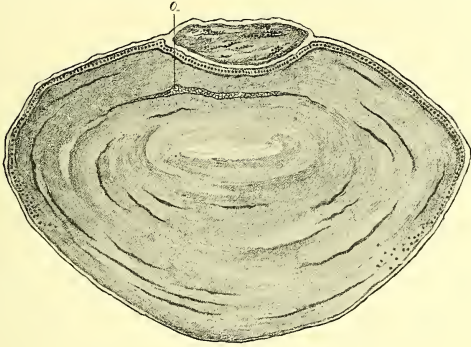


FIG. 290.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xviii. Anterior capsular cataract of eleven years' formation: patch of degenerate lens substance (*o*) deeper than the mass at the anterior pole, giving rise to a second opacity.

presumably caused the anterior capsular opacity and the time when the patient came under observation. The lenses had therefore considerably increased in size, due to the laying on of fresh cortical fibres, subsequent to the time when the anterior polar opacities were formed.

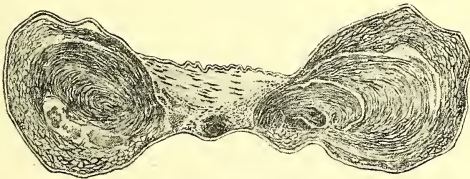


FIG. 291.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xviii. Section of a congenitally malformed lens. It is much flatter than normal, and has a dense anterior capsular opacity.

These fresh fibres would have separated the opaque part, produced by the mass of proliferated epithelium, from the part of the lens which was in contact with them when the disturbance originally occurred, and which was also probably broken up and opaque. In this manner two opacities were formed, separated by clear lens substance, the

posterior of which appeared to sink deeper and deeper as the lens increased in size (Fig. 290).

Regressive changes are always found in old anterior capsular cataracts. All the cells may disappear, though this is rare. Spaces are seen containing granular masses and cholesterin crystals, and often patches of calcareous matter occur. Finally, the whole mass may become so infiltrated with calcareous material that an appearance like stalactites is given (H. Müller).

In the production of anterior capsular cataract by apposition of the lens to a perforated cornea, adhesion of the lens to the cornea may occur. The two subsequently separate more or less, the new-formed connective tissue which binds them together elongating. In this manner a

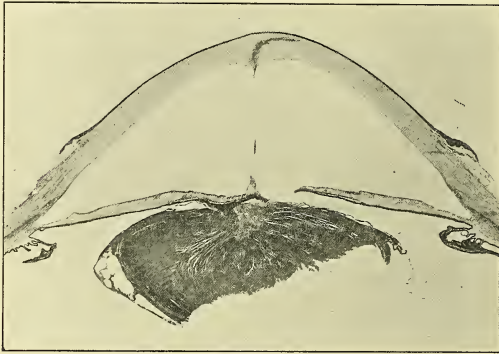


FIG. 292.—PERFORATING WOUND. $\times 7$.

Traumatic cataract, posterior synechia; anterior synechia drawn out into fine thread on re-formation of anterior chamber.

long fine filament may persist, traversing the anterior chamber in an antero-posterior direction (Arlt, Fuchs) (Fig. 292). The filament usually breaks, the ends lying free and becoming gradually absorbed. The traction distorts the lens, so that the anterior part is drawn out into a pyramid—*pyramidal cataract* (Fig. 293). The endothelium of Descemet's membrane may grow on to the sides of the pyramid, and may then form a hyaline membrane (Haring, de Vries). The lens is then seen to be covered by two hyaline membranes, separated from each other by a distinct line; one is the true capsule, lined by cubical cells, the other is a new hyaline membrane, covered by endothelium (Fig. 294).

As regards the causation of anterior capsular cataract, it is usually due to apposition with the cornea as the result of perforation, brought about generally by ulceration—purulent ophthalmia, etc. It is much

more easily produced, *i. e.* by less prolonged apposition to the cornea, in early life, and it would seem that at this period it is not necessary

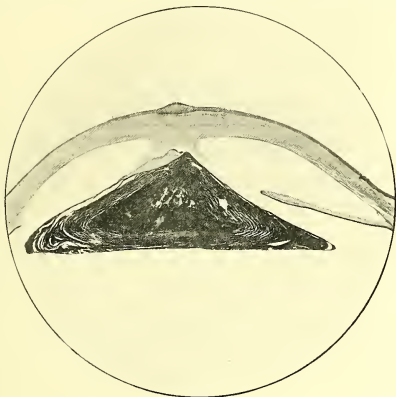


FIG. 293.—PYRAMIDAL CATARACT. $\times 6$.

From a child, æt. 8. Perforation of hypopyon ulcer, following measles. There is a small anterior capsular cataract to the left of the summit.

for the cornea to be inflamed. In later life mere apposition to the normal cornea is not sufficient to produce an anterior capsular cataract :

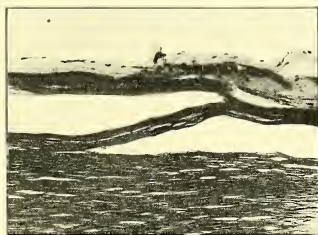


FIG. 294.—PYRAMIDAL CATARACT. $\times 90$.

From the same case as Fig. 293. Showing a double hyaline membrane on surface. The outer membrane is covered with a single layer of endothelium, derived from the cornea ; it is, therefore, of the same nature as Descemet's membrane—a cuticular deposit from the endothelial cells. The inner membrane is the lens capsule.

it is then necessary that the cornea should be ulcerated and perforated, though the same type of cataract may also be formed as the result of

inflammation in the neighbourhood of the lens, *e. g.* in prolonged iridocyclitis, etc. (*v. infra*, "Complicated Cataracts").

True anterior capsular cataract may be congenital and occur in eyes which have apparently perfectly clear corneæ. Two such specimens have been examined microscopically by Treacher Collins. The first had persistent remnants of the anterior vascular sheath of the lens and almost complete aniridia. The second had also congenital anterior synechia and hydrophthalmos; the rest of the lens was imperfectly developed.

Hulke (1857) explains the formation of anterior capsular cataract in early childhood as follows: "When we remember the small size of the anterior chamber of an infant's eye and the spherical shape of the lens at this period of life, it becomes apparent that the distance between the front of the lens and the posterior surface of the cornea must be very small, for a large segment of the lens projects through the pupil and the zenith is considerably in advance of the plane of the iris; in these respects the infant's eye presents a striking similarity to that of the fish. In ophthalmia neonatorum, when the cornea has become inflamed and swollen its posterior surface may actually come into contact with the front of the lens, and then a dot of lymph poured out upon the latter by the inflamed cornea, or even the mere pressure contact, may give rise to opacity by preventing the proper nutritional osmose through the capsule." Treacher Collins considers that the immediate effect of contact is to cause arrest of osmosis—in consonance with Hulke's theory—and that this leads to the lens fibres in the neighbourhood shrinking and breaking up into hyaline globules and detritus. As a consequence of the shrinkage the tension of the capsule at the anterior pole is lessened. There is evidence to show that the only obstacle to more rapid proliferation of the epithelial cells is the tension to which they are subjected. Hence, directly the tension at the anterior pole is lessened they commence to multiply at an increased rate, and form the mass of cells which is the earliest stage of these opacities.

It is not improbable that the mere irritation of contact may suffice to start proliferation, just as the same effect is produced by chronic irritation in eyes with iridocyclitis (Fig. 284), pressure from sarcoma of the ciliary body (Fig. 298). This would be in agreement with the effects of irritation of other epithelial structures. It would also account for the ease with which the condition is brought about in young eyes, whilst with older tissues the stimulus must be more severe or more prolonged.

H. MÜLLER.—Gesammelte Schriften., Leipzig, 1872. KNIES.—K. M. f. A., xviii, 1880. BECKER.—Zur Anat. d. gesund. u. krank. Linse, Wiesbaden, 1883. *TREACHER COLLINS.—T. O. S., xii, 1892; Researches, London, 1896; T. O. S., xviii, 1898. SCHIRMER.—A. f. O., xxxiv, 1, 1888; xxxv, 1, 1889. WAGENMANN.—A. f. O., xxxv, 1, 1889. KRÜGER.—Z. f. A., ix, 1903. GEPNER, JR.—A. f. O., xxxvi, 4, 1890. ARLT.—Die Krankheiten des Auges, Prag, 1855. PAGENSTECHER AND GENTH.—Atlas, Wiesbaden, 1875. HARING.—A. f. O., xliii, 1, 1897. DE VRIES.—A. f. O., liv, 3, 1902. HULKE.—R. L. O. H. Rep., i, 1857. HUTCHINSON.—R. L. O. H. Rep., vi, 1868. NUEL.—A. d'O., xix, 1899. ALT.—T. Am. O. S., 1899. E. v. HIPPEL.—A. f. O., liv, 1, 1902.

POSTERIOR POLAR CATARACTS

The opacities commonly called posterior polar are of two varieties: (1) posterior cortical cataract, which constitutes the earliest phase of most complicated cataracts (q. v.), and (2) an opacity on the back of the posterior capsule—and, therefore, not true cataract at all—due to persistence of part of the posterior vascular sheath of the lens. The histology of these opacities will be discussed elsewhere.

TRAUMATIC CATARACT

When the lens capsule is opened it retracts and the edges roll outwards; the underlying lens fibres, whether wounded or only exposed to the action of the aqueous, swell up so that some protrude from the aperture, and finally break up in the usual manner. These early stages and the final stages have been observed in the human eye, and correspond with those seen in experimental injuries. The intermediate stages have been followed only in experiments which have been carried out by Schlösser and Schirmer.

Immediately after an experimental dissection the iris and the pupillary area of the surface of the lens become covered with a layer of fibrin. This soon disappears except at the site of the wound, where it forms a cap over the swollen lens fibres. In the meshes of the fibrin there are a few leucocytes, often containing pigment granules derived from the iris, free iris pigment, and a few degenerated capsular epithelial cells. As long as the aqueous has access to the fibres vesicular cells are formed amongst them (Schlösser). The epithelium, like that of the cornea, is normally in a state of tension, so that the cells peripheral to the wound are pushed towards it and rapidly cover it. They cease to be regularly cubical and become flattened. It is only after twenty-four hours have elapsed that mitoses are seen (Schirmer), chiefly situated near the edges of the wound, but found also in varying numbers at a distance, and even at the equator. The new-formed cells are more regular, and push their way between the swollen fibres and the fibrin cap. Later, the epithelial cells proliferate in such a manner as to produce a mass of spindle-shaped cells exactly resembling anterior capsular cataract; these cells never show mitoses.

Schlösser describes the formation of a thick mass of fibrous tissue replacing the fibrinous cap, but this is denied by Schirmer. It is probable that Schlösser mistook the nature of the spindle-shaped epithelial cells. Fibrous tissue is never formed under these conditions unless there is coincident injury of the iris or apposition of the lens to the wound in the cornea. In pure lenticular wounds there are no fibroblasts present from which fibrous tissue could be developed.

The subsequent history of the scar is exactly similar to that of a capsular cataract, the nuclei and cells becoming smaller and replaced by a homogeneous matrix. Finally normal cubical cells grow in from the sides under the scar, and form a continuous single layer, which then slowly secretes a hyaline membrane in all respects the same as that found under old anterior capsular cataracts. According to

Schlösser the same process occurs on the anterior surface of the scar. As in the case of Descemet's membrane, the capsule never unites directly, but only occasionally by the formation of a new cuticular membrane.

When the iris is wounded, or when the wound lies partly or entirely behind the iris, not only do leucocytes penetrate into the lens, but fibroblasts also, derived from the iris, as is shown by numerous mitoses in that structure. These cells insinuate themselves between the lens fibres, often carrying pigment granules with them. The connective tissue thus laid down organises into a true fibrous scar (Fig. 292). In human eyes with accidental wounds there is often much inflammatory reaction in the iris and other parts of the eye, and this causes a much greater development of scar tissue, which may anchor the lens to the



FIG. 295.—TRAUMATIC CATARACT. $\times 55$.

Perforating wound; panophthalmitis. Note the disappearance of the anterior capsular epithelium, and the penetration of leucocytes between the lens fibres.

cornea, and also tie down the iris. The corneal and iridic endothelium may then grow over the mass and subsequently develop a hyaline membrane (*cf.* p. 415).

If the wound becomes adequately shut off by fibrin, adhesion of iris, or scar formation, some slight regeneration may occur. The injured fibres are absorbed, but the destructive process goes no farther; new fibres are produced, which are at first arranged irregularly, but tend more and more to assume the normal disposition as the tension within the capsule is re-established.

When the wound is larger more fibres are exposed to the action of the aqueous and break up. Schlösser found that changes occurred in the posterior part of the lens without direct continuity; they commence in a layer parallel to the posterior capsule, between the equator

and the posterior pole, and form spindle-shaped lacunæ filled with finely granular material. Similar lacunæ appear around the nucleus of the lens (perinuclear canals), and in the rays of the anterior star-shaped figure of the lens. According to Schlösser these spaces are connected with each other, and represent a preformed system of lymph channels, carrying lymph from the equator, around the nucleus, and out by the anterior capsule.

Absorption of the lens fibres is largely due to leucocytes in these traumatic cataracts. They become swollen and filled with granules (granule cells, *Körnchenzellen*); they often contain two nuclei. Rarely giant cells may be present.

In man traumatic cataract is very often caused by a septic wound. In these cases the opening in the capsule is filled with polymorphonuclear leucocytes, which penetrate between the fibres far into the substance of the lens (Fig. 295). They doubtless exert a digestive action upon the fibres, which break up and become absorbed with great rapidity; even the capsule may show signs of erosion, though the process is usually so rapid that the eye is lost before the capsule is absorbed. In less acute cases the capsule may become completely absorbed. Leucocytes, with particles of lens capsule within them, have been observed.

LEBER.—*B. d. o. G.*, 1878. DEUTSCHMANN.—*A. f. O.*, xxvi, 1, 1880. BECKER.—*Zur Anat. d. gesund. u. krank. Linse*, Wiesbaden, 1883. SCHLÖSSER.—*Experimentale Studie über traumatische Cataract*, München, 1887. SCHIRMER.—*A. f. O.*, xxxv, 1889. *P. KNAPP.—*Z. f. A.*, iii, iv, 1900; *A. d'O.*, xx, 1900. BOESE.—*Z. f. A.*, ix, 1903.

SECONDARY CATARACT

Secondary or after-cataract is the opacity caused after the extraction of a senile or other cataract. The lens is never regenerated in the

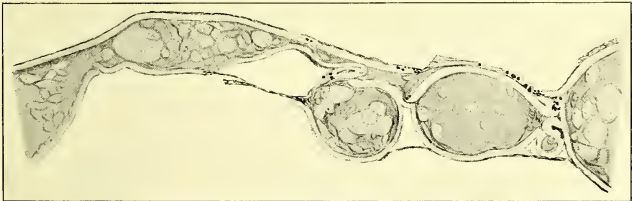


FIG. 296.—SECONDARY CATARACT.
From a specimen by Treacher Collins.

mammalia. After the extraction of a cataract more or less capsule and lens fibres are left behind. The capsule becomes retracted and folded upon itself as the result of its inherent elasticity. The edges of the wound in the anterior capsule become adherent to the posterior capsule or to a greater or less amount of fibrous tissue laid down by fibroblasts

derived from the iris. In this manner a ring of folded capsule, containing more or less of the lens substance, persists behind the iris, whilst the central part, including the pupillary area, is composed of a

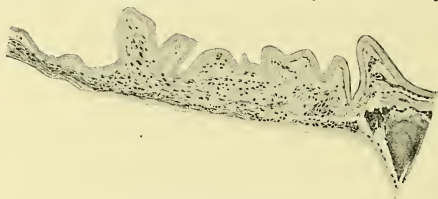


FIG. 297.—SECONDARY CATARACT.
From a specimen by Treacher Collins.

membrane, which may be simply the posterior capsule, or may include a layer of fibrous tissue (Figs. 296, 297, 298).

By the retraction of the capsule the anterior part, lined with cubical epithelium, may be partially dragged backwards, so as to lie posterior at

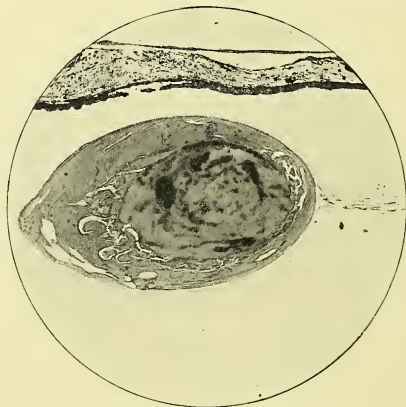


FIG. 298.—REMAINS OF LENS AFTER EXTRACTION. $\times 55$.

From a woman, *æt.* 69, seven years after extraction. Cystoid cicatrix, down-growth of epithelium. There is an epithelial membrane on the anterior surface of the atrophic iris.

the periphery, *i. e.* near the normal position of the equator; this occurs especially when some of the fibres of the zonule are ruptured. Usually there is a considerable remnant of lens fibres enclosed in the folded capsule behind the iris: the same condition is found in old traumatic

cataracts (Fig. 87, Vol. I). Most of these are absorbed, but some generally remain. The cubical cells proliferate and form tissue resembling capsular cataract, or they may form vesicular cells (Fig. 296). In the former case new cuticular membranes are often laid down, which may line not only the anterior, but also the posterior capsule. Irregular new lens fibres are also formed, and these are usually thicker and more sclerotic than normal fibres, and stain more deeply with eosin. They are frequently granular, and their edges are ill defined. The normal equatorial whorl may persist, or may be displaced backwards so as to lie upon the posterior capsule (Wagenmann).

The edges of the wound in the anterior capsule become gradually thinner by absorption, and are often split up into fibres or laminæ.

WAGENMANN.—A. f. O., xxxv, 1, 1889; xxxvii, 2, 1891.

FOREIGN SUBSTANCES FOUND IN THE LENS

The intact capsule is impermeable for anything but fluids; hence foreign material can only enter in the form of solution. In this manner iron is found in cases of siderosis bulbi, caused by prolonged sojourn of fragments of iron inside the globe. In these cases iron-containing pigment, in the form of brown granules, may be found, usually only after wound of the capsule (E. v. Hippel), but also with an intact capsule (Hertel). In the latter case it was chiefly amongst the posterior fibres, and gave the reactions for iron (*see* "Sarcoma of the Choroid").

When the capsule has been wounded formed elements may enter the lens. Leucocytes, connective tissue, and pigment have already been mentioned incidentally. Other cells are those of new growths—glioma (*see* Glioma), sarcoma (*see* Vol. I, p. 368); also epithelial cells in some cases in which the anterior chamber is more or less completely lined with epithelium (*see* Vol. I, pp. 165, 312). Fibrous tissue may undergo further changes inside the lens (*v. infra*, "Ossification of the Lens").

E. v. HIPPEL.—A. f. O., xl, 1, 1894. HERTEL.—A. f. O., xliv, 2, 1897.

Filariæ are said to have been observed in the lens by v. Nordmann (1832) and Gescheidt (1833). As they have never since been found, and the presence of *filariæ* in an evascular structure like the lens is extremely improbable, the statement must be accepted with reserve. The same remarks apply to the trematodes, *Monostoma* and *Distoma* in the lens.

v. NORDMANN.—Mikrographische Beiträge zur Naturgeschichte der wirbellosen Thiere, Berlin, 1832. GESCHIEDT.—v. Ammon's Zeitschrift, iii, 1833. KRAEMER.—In. G.-S., 1899.

COMPLICATED CATARACTS

Complicated cataracts are those occurring as the result of other diseases of the eyeball. They are often called secondary cataracts, but as this term is also used for after-cataracts, following extraction, it is better avoided. The commonest causes of complicated cataracts are

violent inflammations in the anterior section of the eye, *e. g.* *ulcus serpens*, iridocyclitis; chronic inflammations in the posterior section of

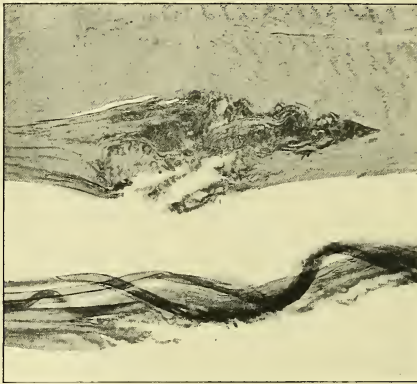


FIG. 299.—POSTERIOR CORTICAL CATARACT. $\times 60$.

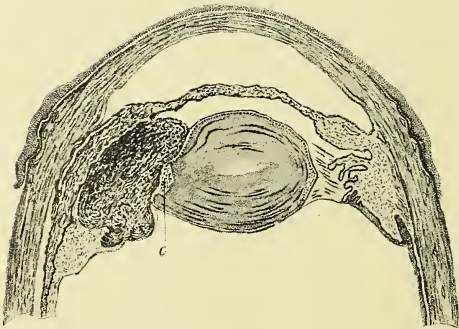


FIG. 300.—ANTERIOR CAPSULAR CATARACT.

Treacher Collins, T. O. S., xviii. Melanotic sarcoma of the ciliary body pressing on the side of the lens, and causing there a subcapsular patch (*o*) similar in appearance to an anterior capsular cataract.

the eye, *e. g.* chronic iridochoroiditis, high myopia, retinitis pigmentosa, detachment of the retina, tumours (Lange, Mitvalsky, Groenouw,

Scherl, Symens), and glaucoma absolutum—*glaucomatous cataract*. Posterior cortical cataracts also occur in glass-blowers (Robinson).

These cataracts result from disordered or deficient nutrition, and vary much in distribution and character, though they eventually become total. In cases where the earliest stages can be studied ophthalmoscopically, such as retinitis pigmentosa or uveitis, it is found that the opacity is usually at first *posterior cortical* in position (Fig. 299); this may be followed or accompanied by an *anterior cortical* cataract. In chronic iridocyclitis, and also in other cases, there is frequently an inflammatory *anterior capsular cataract*. In most cases the whole lens eventually becomes opaque, but differs in appearance and character from an ordinary total senile cataract. Thus, it often shows a yellow or greenish discoloration, the fibres liquefy or become calcified, the



FIG. 301.—DISTORTION OF LENS. $\times 9$.

From a child, æt. 2, after perforation of cornea with scissors.

capsule becomes thickened, and the whole lens is distorted (Fig. 301) or shrunken and tremulous.

The inflammatory anterior capsular cataract does not differ histologically from the simple form; it is often eccentric, situated in the immediate vicinity of the worst foci of inflammation in the iris or ciliary body, and is generally more widely spread, though thinner than the usual form (Fig. 105, Vol. I). There seems also to be more active proliferation of epithelium, which retains its vitality longer, and less frequently gives place to a homogeneous substratum (Figs. 284; 190 and 223, Vol. I), though this also occurs (Fig. 187, Vol. I). The proliferation is most marked when the whole lens is embedded in a mass of cyclitic fibrous tissue; the capsule is then folded, the bays in the curves being filled in with spindle-shaped epithelial cells.

The lens capsule is often absorbed gradually when surrounded by granulation tissue, especially in the presence of giant cells; these

have, indeed, been seen to contain particles of capsule (Wagenmann). Absorption also occurs in panophthalmitis, when the lens is bathed in pus; proliferation of the epithelium does not occur under these circumstances, but only in more chronic conditions. Wagenmann has observed peculiar changes in panophthalmitis associated with old prolapse of the iris. In three out of seven such cases examined there were nucleated fibres at the posterior pole. This has been observed rarely in quite normal lenses (Ginsberg). It is unlikely that the phenomenon is due to proliferation in this situation, or that it is the direct result of the suppuration, since this was always in an early stage. Neither has actual wandering of nuclei been observed in intact fibres. It may be due to the previous perforation of the cornea. Irregular displacement of the nuclei forwards has been observed by van Geuns in the cataract following ligature of vortex veins.

IWANOFF.—Klin. Beobachtungen a. d. Augenheilanstalt zu Wiesbaden, 1861. DEUTSCHMANN.—A. f. O., xxvi, 1, 1880. SCHIRMER.—A. f. O., xxxiv, 1, 1888. WAGENMANN.—A. f. O., xl, 5, 1890. LANGE.—A. f. O., xxxvi, 3, 1890. MITVALSKY.—A. f. A., xxviii, 1894. GROENOUW.—A. f. O., xlvii, 2, 1899. SCHERL.—A. f. A., xxxvi, 1898. SYMENS.—K. M. f. A., xxxix, 1901. KOSTER, GZN.—A. f. O., xli, 2, 1895. VAN GEUNS.—A. f. O., xlvii, 2, 1899. ROBINSON.—Brit. Med. J., 1903. GINSBERG.—Grundriss, Berlin, 1903. ZUR NEDDEN.—Z. f. A., xii, 1904.

Toxic cataracts.—Cataract has been observed to follow poisoning with ergot (Meier, Tepljaschin, Schmidt-Rimpler, and others), naphthalin (Bouchard and Charrin, Hess, Kolinski, Magnus, Faravelli, Klingmann, Mania and Ovio, Helbron), and β -naphthol (van der Hoeve).

The cataract in these cases is secondary to interference with the nutrition of the lens, due to disorder of the circulation in the eye, especially in the choroid (Hess, Klingmann, Faravelli). Mania and Ovio showed that lenses immersed in naphthalin and olive oil do not become opaque. Naphthalin cataract has been the subject of much experimental research.

MEIER.—A. f. O., viii, 2, 1862. TEPLJASCHIN.—In Nagel's Jahresbericht, 1883. SCHMIDT-RIMPLER.—Die Erkrankungen des Auges im Zusammenhang mit anderen Erkrankungen, Wien, 1898. BOUCHARD AND CHARRIN.—Rec. d'O., 1887. HESS.—B. d. o. G., 1887. KOLINSKI.—A. f. O., xxxv, 2, 1889; Arch. de Phys., 1890. MAGNUS.—A. f. O., xxxvi, 4, 1890. FARAVELLI.—Ann. di Ott., xxii, 1893. KLINGMANN.—Virchow's Archiv, cxlix, 1897. MANIA AND OVIO.—Arch. di Ott., vi, 1898. HELBRON.—Z. f. A., ii, 1899. VAN DER HOEVE.—A. f. O., liii, 1, 1901.

LEPROSY

The lens is often cataractous in leprosy, but bacilli are absent (Poncet, Doutrelepont and Wolters, Lie, Neve). Ordinary senile cataract is common.

PONCET.—Progrès méd., 1888; C. f. A., xii, 1888. DOUTRELEPONT AND WOLTERS.—Arch. f. Derm., 1896. *BORTHEN AND LIE.—Die Lepra des Auges, Leipzig, 1899. NEVE.—Brit. Med. J., 1900.

DIABETIC CATARACT

Cataract in diabetics should properly be included in the group of toxic cataracts, since it is due to defects in nutrition caused by the action of toxic metabolic products upon the circulation. It may clear up under general treatment (Nettleship). Ordinary senile cataract may occur in diabetics, and diabetic cataract may differ in no respect from senile cataract, hence there are many difficulties in determining the incidence of the symptom. The numbers given vary from 2 per cent. (Koenig) to 25 per cent. (v. Graefe). Both eyes are almost invariably

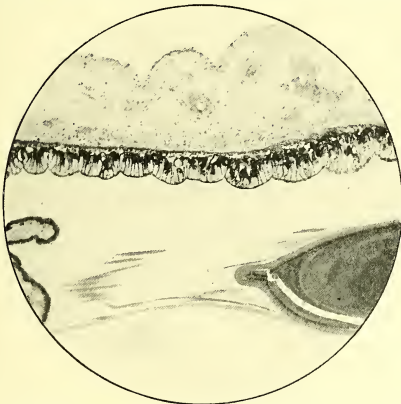


FIG. 302.—REMAINS OF LENS AFTER EXTRACTION. $\times 55$.

From a specimen by Prof. Wintersteiner. The patient was a diabetic; note the diabetic oedema of the retinal pigment epithelium of the iris (*see* Vol. I, p. 319). Note the suspensory ligament and the cubical epithelium lining the lens capsule.

affected (54 out of 56 cases, Zeller), though often in different degree. The youngest case on record was a girl, $\text{aet. } 5$ (Frey); it may occur at any greater age.

Diabetic cataract has been examined microscopically by Knapp, Becker, Deutschmann, Kamocki, and Goerlitz. The changes are those found in other types of cortical cataract. Unlike these, however, they begin close under the capsule; the nuclei of the epithelium stain unequally or are replaced by vacuoles. The lens fibres are separated by spaces containing coagula and the usual cataractous products. According to Deutschmann and Kamocki the death of the epithelium leads to pathological diffusion through the capsule. Vesicular cells are generally present, especially at the equator.

The fundamental cause of diabetic cataract is obscure. It is not due to diabetic cachexia, since the patients are often well nourished;

the condition is not commoner in advanced cases, and it is occasionally unilateral. It has been attributed to deleterious matter in the aqueous (Frerichs, Lohmeyer). Sugar may form lactic acid in the aqueous. Lohmeyer's observation that this fluid is acid in diabetic cataract has not, however, been confirmed; it was found to be alkaline by Leber and Deutschmann, neutral by Jany. Moreover, diabetic cataract does not invariably commence at the periphery under the capsule.

More probable, *à priori*, was the view that the sugar itself in the lymph of the eye caused the complaint. Kunde, Richardson, and others have produced lenticular opacity by large doses of sugar or sodium chloride; it has also been caused by injection of strong solutions into the anterior chamber. The opacity is due to abstraction of water from the lens, and at least 5 per cent. of sugar is necessary. The aqueous never contains anything approaching this amount in diabetes: Deutschmann found 0.5 per cent. in the aqueous, 0.366 per cent. in the vitreous in a child who had been passing 8 per cent. in the urine. Further, the cornea is made opaque by these strong solutions (Deutschmann, Bono), and the microscopical changes found in these artificial cataracts are totally different from those found in diabetic cataract. The lens usually contains traces of sugar, but it may be absent entirely. It may be present in one eye and absent in the other (Deutschmann).

It is therefore probable that the disorder of nutrition of the lens which causes diabetic cataract is due to some unknown deleterious agent circulating in the blood and lymph streams.

LOHMEYER.—Z. f. rat. Med., v, 1854. KUNDE.—Z. f. wissenschaft. Zool., viii, 1857. v. GRAEFE.—A. f. O., iv, 2, 1858. RICHARDSON.—Med. Times and Gaz., 1860. LEBER.—A. f. O., xxi, 3, 1875. DEUTSCHMANN.—A. f. O., xxiii, 3, 1877; xxv, 2, 1879; xxxiii, 2, 1887. JANY.—A. f. A., viii, 1879. BONO.—C. f. A., vii, 1883. NETTLESHIP.—T. O. S., v, 1885. FREY.—London Med. Record, 1887. MAGNUS.—A. f. O., xxxvi, 4, 1890. KAMOCKI.—A. f. A., xvii, 1887; xxv, 1892. SEEGEN.—Der Diabetes mellitus, Berlin, 1893. GOERLITZ.—Dissertation, Freiburg, 1894. KOENIG.—C. f. A., xxi, 1897. HEINE.—A. f. O., xlv, 3, 1898. WILLIAMSON.—Diabetes mellitus, Edinburgh, 1898. ZELLER.—Dissertation, Tübingen, 1899. GROENOUW.—In G., S., 1902 (Bibliography).

CHANGES IN THE SUSPENSORY LIGAMENT

Little is known of the histological changes which occur in the zonule of Zinn in pathological conditions. In panophthalmitis the digestive action of the leucocytes is exerted upon the fibres, so that they are destroyed and luxation of the lens takes place: this has been observed in metastatic ophthalmitis (Vossius, Herrnheiser, and Ginsberg). Similar changes, though less rapidly produced, may occur when the zonule is invaded by granulation tissue in cyclitis, or by malignant growths—glioma (q. v.) (da Gama Pinto, Wintersteiner, Knapp), sarcoma (q. v.). The fibres of the zonule are often thickened in chronic inflammatory conditions (Kostenitsch), *e. g.* after extraction of senile cataract. Stretching of the fibres, with or without thickening, is observed in buphthalmia (E. v. Hippel, Brunnhuber), though it may be absent (Grahamer); and also in staphylomatous conditions, whether corneal or ciliary (Panas, Fuchs). The stretching in these cases

causes the characteristic flattening of the lens (Figs. 102 and 107, Vol. I). Congenital malformations, ruptures, etc., will be considered elsewhere.

GARNIER.—A. f. A., xxiv, 1892. TREITEL.—A. f. O., xxvi, 3, 1880. KOSTENITSCH.—A. f. O., xxxvii, 4, 1891. WAGENMANN.—A. f. O., xxxvii, 2, 1891. E. v. HIPPEL.—A. f. O., xlv, 3, 1897. BRUNNHUBER.—K. M. f. A., xv, 1877. GRAHAMER.—A. f. O., xxx, 3, 1884. PANAS.—*Traité*, Paris, 1894. FUCHS.—Textbook, London, 1899. * BEDNARSKI.—A. f. A., li, 1905.

CALCIFICATION AND OSSIFICATION

Calcification of the lens may occur within the intact capsule, and is often found in the final stages of complicated cataracts, in shrunken globes, and sometimes in diabetic cataract. Partial calcification is always seen in old anterior capsular cataracts.

Ossification of the lens can only occur after rupture or wound of the capsule, since only under these conditions can osteoblasts obtain access to the interior. The first case was reported by Gluge. H. Müller and Knapp denied the possibility of ossification; Virchow doubted it; and Berthold considered that it had not been demonstrated. There is no question that it occurs in old cases of shrunken globe after rupture or absorption of the capsule, and invasion of the lens by connective tissue of cyclitic origin. Cases have been recorded by Goldzieher, Alt, Panas, and others, and the condition is not very uncommon. The formation of bone exactly follows the course taken in the choroid (q. v.) and in cyclitic membranes (q. v.).

GLUGE.—Ann. d'Oc., x, 1843. BERTHOLD.—A. f. O., xviii, 1, 1872. BERGER.—A. f. O., xxxix, 4, 1883. SICHEL.—Ann. d'Oc., cxii, 1884. ROMANO-CATANIA.—Arch. di Ott., ii, 1895. DUNN AND HOLDEN.—A. of O., xxvii, 1899. LAGRANGE.—*Tumeurs de l'Œil*, i, Paris, 1901. WERNCKE.—K. M. f. A., xli, 1903. ZIA.—Z. f. A., xii, 1904. AUBINEAU.—Ann. d'Oc., cxxxii, 1904.

CHAPTER VIII

THE VITREOUS

THE NORMAL VITREOUS

THE vitreous is an inert, jelly-like structure, which subserves optical functions. In pathological conditions, so far as is known, it is purely passive. It is therefore advisable to avoid such expressions as "shrinking of the vitreous," etc., which imply an activity which it does not possess, and it is incorrect to use such terms as "hyalitis," etc.

The normal vitreous contains about 99 per cent. of water. Its structure can only be determined by special methods of preparation. Retzius recommends 3 per cent. bichromate, Flemming's solution, or 1 to 2 per cent. sublimate for hardening; most early authors and Salzmann used Müller's solution. It is found to consist of a delicate framework with sparse cells.

The framework consists of fine granular fibrils forming a network, the meshes of which are smaller towards the periphery. The fibrils stream out in large numbers from the neighbourhood of the ora serrata or slightly anterior (Salzmann). At the periphery they are attached to the extremely thin *membrana hyaloidea*, which lies upon the inner surface of the retina. At the edges of the disc the hyaloid membrane passes forward, forming the *canal of Cloquet*, about 2 mm. wide, which in foetal life contained the hyaloid artery; it persists as a lymph space. The canal ceases at about the middle of the vitreous, being continued forwards to the back of the lens only in the form of rather denser fibrils. The presence or absence of a definite hyaloid membrane behind the lens has given rise to much discussion. It is also doubtful if there is a definite internal limiting membrane to the retina other than the hyaloid membrane, which must be considered part of the vitreous. The decision of these points depends chiefly upon the embryology of the vitreous, which is a subject of great dispute (*cf.* Kölliker, Kessler, Keibel, Retzius, Lenhossék, Cirincione). In old age most of the fibrils seem to disappear, whilst others, especially in the ciliary region, become thickened.

The cells are very sparse, and are chiefly distributed in the peripheral parts (subhyaloid). They are round or star-shaped, with one or two nuclei; the cytoplasm is often vacuolated (physaliphores). There

are a few wandering cells, and Schwalbe considers that all the cells are leucocytes.

BOWMAN.—Dublin Quarterly Jl. of Med. Sc., 1848. IWANOFF.—A. f. O., xv, 2, 1869. RETZIUS.—Biologische Untersuchungen, vi, 1894. SALZMANN.—Die Zonula ciliaris u. ihr Verhältniss z. Umgebung, Leipzig and Wien, 1900. KÖLLIKER.—Entwicklungsgeschichte, Leipzig, 1861; Zeit. f. wiss. Zool., lxxvi, 1904. KESSLER.—Zur Entwicklung des Auges der Wirbelthiere, Leipzig, 1877. KEIBEL.—A. f. Anat. u. Phys., 1886. LENHOSSÉK.—Die Entwicklung des Glaskörpers, Leipzig, 1903. CIRINCIONE.—C. f. A., xxvii, 1903; La Clinica oculistica, 1904; A. f. A., l, 1904.

FLUIDITY OF THE VITREOUS

Fluidity of the vitreous is due to inflammatory or degenerative absorption of the fibrils. The substance itself also undergoes changes, whereby it becomes liquid instead of viscous. Moreover, it is altered chemically, as is shown by the deposition of crystals—cholesterin, fats, phosphates. The condition is common, occurring in cyclitis, glaucoma, myopia, etc. It may be total or partial; partial liquefaction is frequent in old age, when irregular cavities containing fluid are found, and in myopia, when the fluid part is generally at the posterior pole (Weiss). Cholesterin is common in the fluid vitreous—*synchysis scintillans* (cf. Tangeman). I have also seen it in an apparently normal eye with firm vitreous.

WEISS.—Mittheilungen aus der ophth. Klinik zu Tübingen, i, 1882; ii, 1884. TANGEMAN.—A. of O., xvii, 1888.

DETACHMENT

Detachment of the vitreous is usually due to the shrinkage of inflammatory products, which have been poured out into it from the ciliary body, choroid, or retina. Probably the cases which have been described in which the hyaloid remains attached to the retina are really cases of fluid vitreous. It is difficult to decide whether the detachment is *intra vitam* or *post mortem*.

The vitreous may be detached from the posterior pole, either in small degree or until it lies as a hemispherical mass behind the lens (globular detachment, Milles) (Fig. 305). It is often tent-shaped (infundibular detachment, Milles) (Figs. 303, 307), the apex of the cone being at the disc, or at a wound by a foreign body somewhere in the retina, or anterior at the site of a perforating wound. The detached vitreous always contains foreign inflammatory elements, and usually organising connective tissue often mixed with blood. The outer surface is generally covered with an endothelial membrane, which may consist of several layers, and is exactly similar in origin and appearance to membranes found on the retina (*v. infra*). The cells may deposit fine hyaline membranes, which show a considerable amount of resistance. There may be a layer of connective or fibrous tissue, either loose and reticular or dense. The subhyaloid space is filled with extravasated lymph, which does not usually coagulate; it may contain blood.

Antero-lateral detachment is occasionally seen, the vitreous being

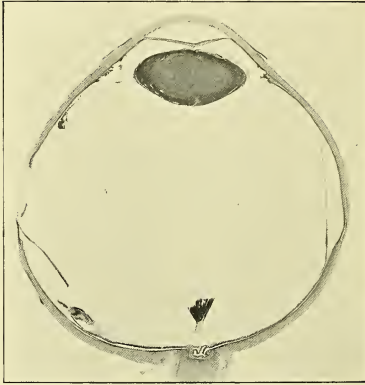


FIG. 303.—DETACHMENT OF THE VITREOUS. $\times 3$.

From a man, æt. 40; glaucoma. Note the hyaloid membrane from ora serrata to disc; blood-clot at the apex, near disc. Note also optic cup filled with folded, cystic retina (Parsons, T. O. S., xxv).



FIG. 304.—DETACHMENT OF THE VITREOUS. $\times 55$.

From the same specimen, showing the thickening of the hyaloid membrane.

separated from the suspensory ligament (Fig. 307). Detachment of the vitreous may be due to several causes :

(1) Pushing forwards, as in cases of subhyaloid hæmorrhage.

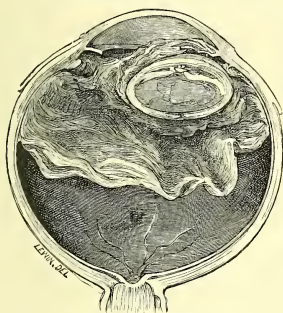


FIG. 305.—DETACHMENT OF THE VITREOUS.

R. L. O. H. Museum. From a man, æt. 56 ; traumatic dislocation of lens, globular detachment of vitreous, which passes forwards into the anterior chamber.

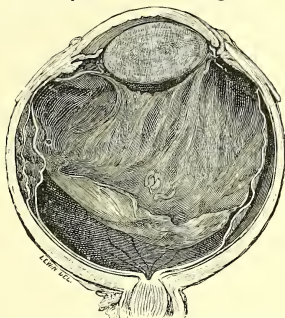


FIG. 306.—DETACHMENT OF THE VITREOUS.

R. L. O. H. Museum. Ruptured globe, prolapse of iris, displacement of lens, partial detachment of vitreous and choroid.

(2) Detachment *e vacuo* (Iwanoff), as in myopia, anterior staphyloma, sometimes in glaucoma, and possibly after cataract extraction

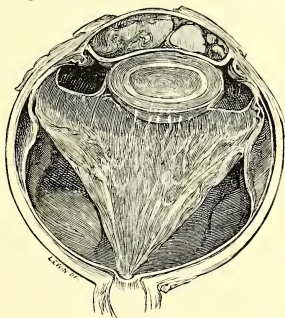


FIG. 307.—DETACHMENT OF THE VITREOUS.

R. L. O. H. Museum. From a man, æt. 61 ; injured five weeks previously with chip of iron. Ulceration of cornea, pus and blood in a.c., retraction of iris and lens, antero-lateral and infundibular detachments of vitreous.

owing to exudation of fluid from atheromatous retinal vessels. According to Elschnig, detachment of the vitreous does not occur in myopia.

(3) Pulling forwards. This is by far the commonest cause, and is due to the shrinking of exudates—fibrin (Leber) etc.—or of organising connective tissue in the vitreous.

H. MÜLLER (1856).—*Gesammelte Schriften*, Leipzig, 1872. IWANOFF.—*A. f. O.*, xv, 2, 1869. HERZOG CARL THEODOR.—*A. f. O.*, xxv, 3, 1879. TREITEL.—*A. f. O.*, xxvi, 3, 1880. LEBER.—In Treitel, *loc. cit.* WEISS.—*Mittheilungen a. d. ophth. Klinik zu Tübingen*, i, 1882; ii, 1884; *A. f. O.*, xxxi, 3, 1885. MILLES.—*R. L. O. H. Rep.*, xi, 1886. NORDENSON.—*Die Netzhautablösung*, Wiesbaden, 1887. *ELSCHNIG.—*K. M. f. A.*, xlii, 1904. PARSONS.—*T. O. S.*, xxv, 1905.

ABNORMAL PRODUCTS IN THE VITREOUS

Inflammatory products.—These have already been referred to in treating of cyclitis (q. v.). They also occur in retinitis and especially

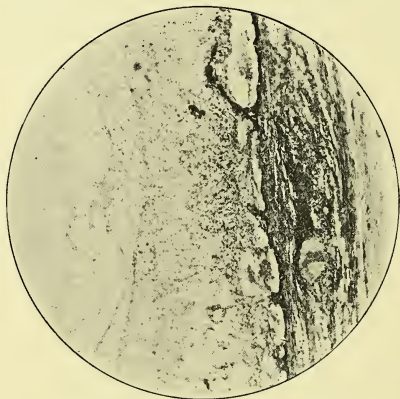


FIG. 308.—PANOPHTHALMITIS. $\times 60$.

After needling: exudates and leucocytes in the vitreous.

in choroiditis, even in the absence of clinical signs of cyclitis. The opacities in the vitreous in myopia, choroiditis, etc., are caused by inflammatory products; they are chiefly exudates which have passed through the retina. Whether leucocytes are derived from the same source and enter the vitreous in the same manner is open to doubt; it is more probable that they come from the ciliary body, even when the evidences of cyclitis are minimal or absent. In these conditions no true organisation of the inflammatory products occurs, and they remain unchanged in nature for an indefinite time, though they may increase in quantity. This fact affords further evidence that leucocytes play no integral part in the organisation of exudates, and it also militates against the view that the cells of the vitreous can proliferate and form fibrous tissue. It is unlikely that leucocytes can pass through the uninjured choroid

and retina; the membrane of Bruch is probably an absolute barrier as long as it is intact, a view which is supported by the histological changes in retinochoroiditis (q. v.). Vitreous opacities may be absent in many types of severe choroiditis. They are most numerous in this disease when the inflammation attacks the peripheral part of the fundus—in fact, when implication of the ciliary body is most likely to occur. In any case it is certain that inflammatory products in the vitreous are most common and greatest quantitatively in acute and chronic cyclitis.

The nature and arrangement of the cells in the vitreous in cyclitis have already been sufficiently indicated. In purulent cyclitis polymorphonuclear leucocytes form the bulk of the exudates. They are often deposited in layers, owing to the manner in which they are

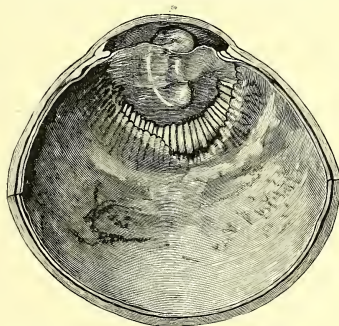


FIG. 309.—ATYPICAL DETACHMENT OF RETINA

R. L. O. H. Museum. About two thirds of the anterior half of the right eye of a man, æt. 35. Sight destroyed in childhood. Upper part of cornea staphylo-matous. Lens shrunken, forming a flattened mass attached to the back of the cornea. Ciliary processes concealed by a fold of retina prolonged forwards from the ora serrata; indentations of ora serrata much increased in size.

extruded from the blood-vessels and to the character of the lymph-streams, and not to any structural peculiarity of the vitreous itself. As the condition passes into one of panophthalmitis the vitreous becomes more and more pervaded with the cells, and their exact distribution depends upon the special nature of the case (Fuchs) (*see* "Purulent Choroiditis"). Finally the whole vitreous is converted into an abscess; rarely multiple abscesses may occur. As in wounds of the retina, etc., the reactive proliferative changes vary inversely with the acuteness and virulence of the inflammation, so that a capsule of fibrous tissue is the most which is seen in infective cases, and this only rarely. In severe cases most of the cells necrose and break down into amorphous granular masses.

The cells of the vitreous have been held to take an active part in the production of the cellular exudates. It is probable that the changes

which have been described occur, not in any special cells of the vitreous, but in leucocytes. Karyomitosis has been described, but usually multiplication is by direct division, such as has been observed elsewhere in leucocytes. Most of the changes are undoubtedly degenerative, nearly all the new cells being derived from the ciliary or retinal vessels by diapedesis. The cells are often round or star-shaped, and may be signet-ring-shaped (physaliphores) from the development of vacuoles, which may be fatty (*see* "Wounds of the Retina"). Besides the common organisms found in suppurative conditions in the eye, the aspergillus, and possibly other fungi, have been observed rarely in the vitreous (Schirmer, Nobbe, Römer, Kampherstein).

Inflammatory products also occur in non-suppurative cyclitis,

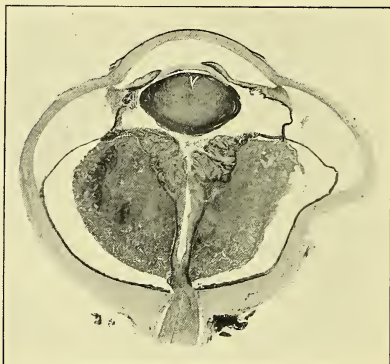


FIG. 310.—PHTHISIS BULBI. $\times 3$.

From the same specimen as Figs. 190, 285. Retraction of periphery of iris, total posterior synechia: anterior capsular cataract: detachment of ciliary body: detachment of retina: sub-retinal coagulum: choroid *in situ*: grooves in sclerotic due to pressure of recti.

e. g. in syphilis. The plastic exudate shows the greatest tendency to organise, so that membranes and masses of fibrous tissue are formed behind the lens, often encapsulating it, whilst offshoots pass back to be attached to the retina (*see* "Cyclitis"). As these deposits organise they contract, so that the retina is pulled up and detached from the choroid. It remains attached at the ora serrata and at the optic disc, so that a tent-shaped detachment is at first produced; if the retina is adherent to the choroid at any other spot, as at the site of a wound or patch of retinochoroiditis, it also remains attached here. Ultimately the traction may be so great as to tear the retina away at such spots, in which case a hole is formed. As the fibrous tissue contracts still more the periphery of the retina is dragged forwards and inwards behind the lens.

Here in the anterior part it is usually folded into a thick mass, whilst the posterior part stretches back to the disc as a straight, unfolded, central band. The inner surface of the retina thus comes to be applied anteriorly to the *pars plana* of the ciliary body and to a transverse cyclitic membrane or mass of organised tissue, rarely to the back of the lens, whilst posteriorly it is gathered up into the central band (Fig. 310). The shrunken vitreous is thus replaced by organised fibrous tissue, which may contain giant cells, fatty globules, cholesterin, pigment cells, and free pigment, calcareous deposits, and eventually bone. Meanwhile the eye has been shrinking, so that the vitreous chamber is reduced to the smallest possible space (Figs. 190, 223, Vol. I).

It has already been stated that primary "hyalitis" (Straub) is an impossibility. This is due to the fact that after foetal life the vitreous contains normally no vessels. Moreover, it is by no means certain that it contains fixed cells, and if it does these are very scanty in numbers, and there is no evidence that they are capable of proliferating. "Hyalitis" (Schmidt-Rimpler) may indeed be used to describe the condition of inflammatory infiltration of the vitreous in the absence of signs of previous purulent cyclitis or choroiditis, but the term is much best avoided, owing to its ambiguity and the inaccuracy of the ideas to which it may give rise.

IWANOFF.—A. f. O., xv, 2, 1869. SCHMIDT-RIMPLER.—B. d. o. G., 1878. WAGENMANN.—A. f. O., xxxiv, 1889. AXENFELD.—A. f. O., xl, 3, 1894. BAAS.—A. f. O., xlv, 3, 1897. STRAUB.—IX International Congress, Utrecht, 1899; Z. f. A., ii, Ergänzungsheft, 1899. PARSONS.—R. L. O. H. Rep., xv, 1903. FUCHS.—A. f. O., lviii, 3, 1904. SCHIRMER.—A. f. O., xlii, 1, 1896. NOBBE.—A. f. O., xlv, 3, 1898. RÖMER.—K. M. f. A., xl, 1902. KAMPFERSTEIN.—K. M. f. A., xli, 1903.

Tumours.—Tumour-cells may be carried into the vitreous, and may even set up metastatic deposits there. This occurs most frequently in glioma retinae (q. v.), and is indeed the rule in glioma endophytum. It is rare in other tumours, but has been described in a case of melanotic sarcoma of the iris, which had extended so as to involve the ciliary body and choroid (Ewetzky). A carcinomatous deposit between two ciliary processes has been described by v. Michel in a case of metastatic carcinoma of the choroid.

EWETZKY.—A. f. O., xlii, 1, 1896. v. MICHEL.—Festschrift d. phys.-med. Gesellschaft, Würzburg, 1892.

Blood.—Hæmorrhage into the vitreous may occur spontaneously in arteriosclerosis or inflammation of the retina (q. v.), or from wounds or injuries of the ciliary body or retina and choroid, or from new-formed vessels in the vitreous. Hæmorrhages from the retina may be subhyaloid, or may burst through the hyaloid membrane and invade the vitreous. The hæmorrhage may be severe, as in the expulsive hæmorrhage which sometimes follows the relief of tension in glaucoma, etc. Smaller hæmorrhages may be slowly and completely absorbed by the solution of the fibrin and the removal of the broken-down corpuscles and colouring matter by leucocytes, or in rare cases they may organise (see "Retinitis proliferans"). The blood-clots formed by perforating wounds or foreign bodies become partly absorbed and partly organised

(see "Wounds of the Retina"). There is no evidence that the cells of the vitreous take any part in the process of organisation.

Large clots may contract so much that the vitreous becomes detached. They are then often surrounded by an endothelial membrane, which usually consists of a single layer of cells, but may be laminated.

PARASITES

Cysticercus occurs in the eye relatively commonly in some countries, notably Germany; it is rare in England, France, Austria, etc. v. Graefe saw 90 cases in 80,000 cases of eye disease, de Wecker 2 in 100,000. The variations are due to the geographical distribution of the cysticercus and its tænia, the tænia solium. It occurs at all ages, most from 21 to 30 (Hirschberg), and rather more frequently in males (v. Graefe, Leber).

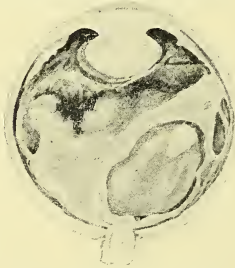


FIG. 311.—INTRA-OCULAR CYSTICERCUS.

Hill Griffiths, T. O. S., xvii. Section of eyeball with cysticercus in the vitreous; head retracted.

The cysticercus is usually solitary in the eye, and attacks only one eye, generally the left. It may be primarily in the vitreous, but more commonly it is subretinal, making its way through the retina into the vitreous—1 : 2 (v. Graefe), 12 to 16 cases (Hirschberg). In 20 cases examined anatomically, 10 were subretinal, 10 intra-vitreous. The size varies with the duration—from $1\frac{1}{2}$ mm. to 9 mm.; largest 15 mm. in diameter (Hirschberg, Leber). The duration of life of the cysticercus is at least two years, probably three to four years. The cyst is usually spherical, occasionally oval; the head and neck of the cysticercus cellulosæ can be seen when extended; spontaneous movements are of supreme diagnostic importance.

Eyes containing cysticercus cysts have been examined in 30 or 40 cases; 29 most important cases have been collected and set down in detail by Kraemer. In these cases 13 were subretinal, 11 preretinal (in one free in the middle of the vitreous), 3 intra-retinal, and once the cysticercus could not be found, though seen ophthalmoscopically (Warnecke). In all cases there was partial or complete detachment of the retina. In 6 cases there was circumscribed formation of bone—once in the actual cysticercus capsule (Saemisch), twice in tissue uniting the retina and choroid, once in degenerated retina, and twice in the choroid (Wagenmann, Peschel).

Suppuration immediately around the cyst was found in 7 cases. In 4 cases giant cells were found (Schröder and Westphalen, Dolina, Wagenmann, Heldmann)—once in the centre of an absorbed cyst, once on the inner surface of the retina, once in the chitinous membrane, once in the granulation tissue surrounding the cyst: Hirschberg

and de Vincentiis found giant cells in the true capsule in several other cases.

The cysticercus acts as a foreign body, and invariably sets up

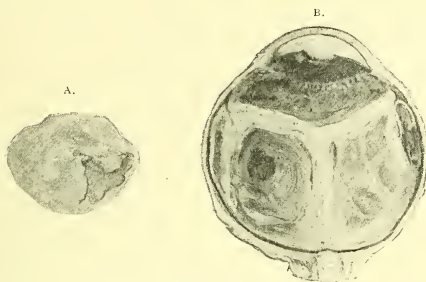


FIG. 312.—INTRA-OCULAR CYSTICERCUS.

Hill Griffiths, T. O. S., xvii. Subretinal cysticercus.

chronic inflammatory reaction, with leucocytosis and proliferation of connective tissue. In a small number of cases the process goes on to suppuration, usually only at a late stage—from the beginning of failure of sight to pus formation, 3 to 15 months (v. Graefe), 6 to 18 months (Leber). Leber regards the process as due to secondary invasion of micro-organisms into an area of diminished resistance; the tissues have, however, been found free from organisms in the absence of operative procedure (Kraemer). Baumgarten, on the other hand, found organisms in the tissues around the cyst, but not in the operation wound (in Treitel's case). Probably the suppurative process is usually of a non-bacterial nature, brought about by a summation of chemical stimuli; this accounts for its remaining localised, and leading eventually to an encapsuled abscess.

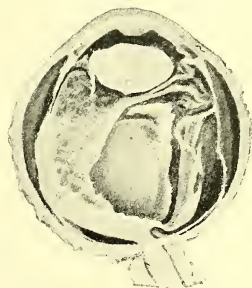


FIG. 313.—INTRA-OCULAR CYSTICERCUS.

Hill Griffiths, T. O. S., xvii. Cysticercus in the vitreous; head and neck extended.

In one case (Pilgrim) the site of invasion of the parasite could be anatomically demonstrated in a posterior ciliary vessel. In Stölting's case the new-formed capsule consisted of thickened retina, but the choroid may also take part (Saemisch).

COCCIUS.—Die Anwendung d. Augenspiegels, Leipzig, 1853. V. GRAEFE.—A. f. O., i, 1, 1854; ii, 1, 1855; iii, 2, 1857; iv, 2, 1858; vii, 2, 1860; xii, 2, 1866; xiv, 3, 1868. SOELBERG WELLS.—R. L. O. H. Rep., iii, 1862. TEALE.—R. L. O. H. Rep., v, 1866.—

HIRSCHBERG.—Virchow's Archiv, xlv, 1869; A. f. A., i, 1870; ii, 1871; A. f. O., xxii, 3, 4, 1876; B. z. A., iii, 1878; C. f. A., iii, 1879; ix, 1885; x, 1886; xvi, 1892; xvii, 1893. HULKE.—T. O. S., iii, 1883. SINCLAIR.—Brit. Med. J., 1883. VERNON.—Lancet, 1883. LEBER.—A. f. O., xxxii, i, 1886. PILGRIM.—Dissertation, München, 1888. v. SCHROEDER AND WESTPHALEN.—A. f. O., xxxv, 3, 1889. DOLINA.—Ziegler's Beiträge, v, 1889. SALZMANN.—K. M. f. A., xxix, 1891. WAGENMANN.—A. f. O., xxxvii, 3, 1891. WARNECKE.—Dissertation, Göttingen, 1893. MITVALSKI.—C. f. A., xvii, 1893. PINCUS.—A. f. O., xl, 4, 1894. CHEATHAM.—Ann. of Ophth., iii, 1894. HILL GRIFFITH.—T. O. S., xvii, 1897. PESCHEL.—Nagel's Jahresbericht, 1897. *KRAEMER.—In G.-S., 1899 (Bibliography).

Echinococcus has been found inside the eye in two undoubted cases only (Hill Griffith, Werner). An old case, published by Gescheidt,

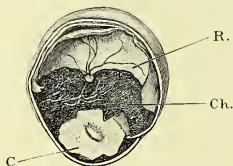


FIG. 314.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Posterior half of eyeball. R. Retina. Ch. Choroid. C. Cyst.

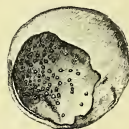


FIG. 315.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Cyst, natural size, showing brood-capsules in the interior.

(1833), is open to doubt. The clinical features of the two cases were similar. In both the cyst was visible as an opacity on the posterior

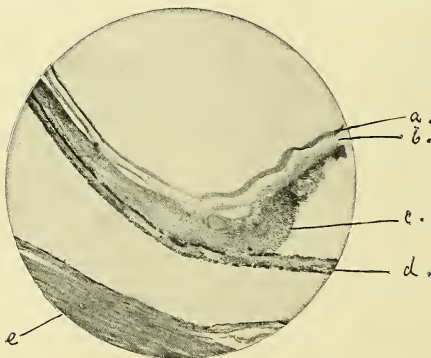


FIG. 316.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Cyst adherent to choroid. a. Parenchyma of cyst. b. Hyaline laminated ectocyst. c. Layer of connective tissue and exudation. d. Choroid. e. Sclerotic.

surface of the clear lens, and appeared closer to the observer than a posterior cataract. There was no red reflex, and the eye was blind.

In Werner's case the tension was raised; in Hill Griffith's glaucoma was induced by atropin.

Anatomically both were simple cysts, containing no daughter cysts

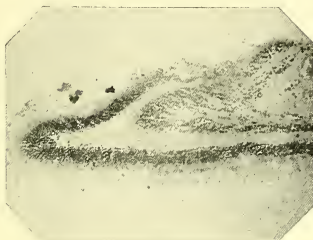


FIG. 317.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Free edge of retina, showing doubling back of nuclear layers.

as distinguished from brood capsules; each completely filled the eye behind the lens. One was situated in the vitreous, the other between

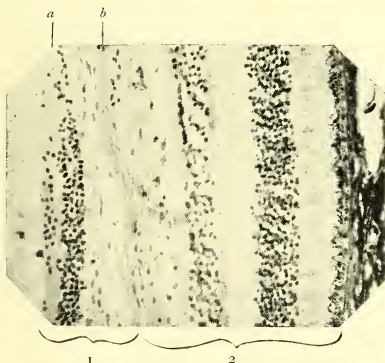


FIG. 318.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Retina a few millimetres from free edge. 1. Degenerated lower half, detached by cyst. *a*. Remains of nuclear layers. *b*. Line of contact of internal limiting membrane. 2. Upper half of retina, in normal position.

the retina and the choroid. Probably the difference in situation accounted for the sterility of the former, and the contact of the latter with the vascular choroid possibly led to a better state of nutrition and

promoted the development of brood capsules (Werner.) In neither case was a connective-tissue capsule present.

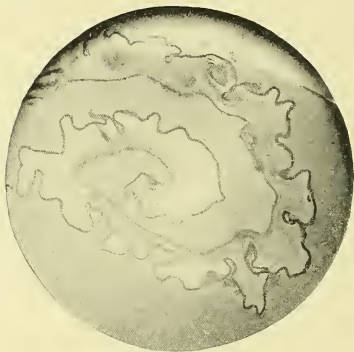


FIG. 319.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Hyaline laminated ectocyst, curved inwards. The outer surface is greatly wrinkled.

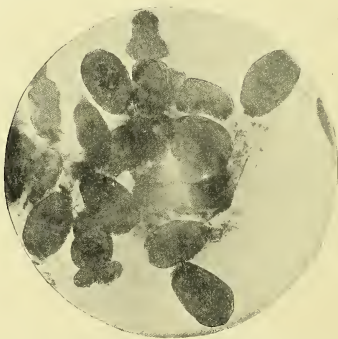


FIG. 320.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Ruptured brood capsule, showing scolices, the majority with rostellum retracted. One can be seen above with rostellum and hooks evaginated, and the suckers on each side.

As regards the mode of infection, while cysticercus can be caused by auto-infection, this is impossible in the case of hydatid, since the *Tænia echinococcus* has never been seen in man.

In Werner's case the cyst was a typical echinococcus. It consisted of two layers—an outer, thick, homogeneous, and elastic, with a great tendency to curl inwards, and composed of numerous fine laminæ (Fig. 316) and an inner or parenchymatous layer (endocyst) much



FIG. 321.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. *a*. Section of cyst from Hill Griffith's case, showing ectocyst only. *b*. Section from Werner's case, showing granular parenchyma above the ectocyst.

more delicate, and composed of a finely granular substance containing many nuclei, but no outlines of any cells (Fig. 321, *b*). It is traversed by a fine network of stiff homogeneous cords, seen only in surface preparations. There were small white bodies on the inner surface, which proved to be brood capsules; they arise from the parenchyma, and are connected with it by a narrow stalk. In some of them Werner counted as many as fifteen heads or scolices. Fig. 320 represents a capsule ruptured by pressure, with scolices set free. Some are retracted, the circle of hooklets being visible in their interior, while others are fully extended, and show their structure very well, viz. the rostellum with hooklets, four suckers, and below this a neck-like constriction. Each head is attached to the inner surface of the capsule by a small stalk which passes into its base. Heads in an early stage of development can be seen in most of the capsules. In order to give an idea of the size of a scolex, the hook of a cysticercus has been placed by the side of one of them (Figs. 322, 323).



FIGS. 322 AND 323.—INTRA-OCULAR HYDATID CYST.

Werner, T. O. S., xxiii. Showing relative sizes of echinococcus head and hook from cysticercus.

GESCHEIDT.—v. Ammon's Zeitschrift, iii, 1833. HILL GRIFFITH.—T. O. S., xvii, 1897.
*WERNER.—T. O. S., xxiii, 1903.

Filariae have been observed in the vitreous ophthalmoscopically by Quadri (1858), Fano (1868), Schöler (1875), and Eversbusch (1891); the observations are open to much doubt. They are, however, sub-

stantiated by the confirmation of an ophthalmoscopic examination with the microscope by Kuhnt (1888). The case is reported in full by Kraemer.

KUHNT.—A. f. A., xxiv, 1892. KRAEMER.—In G.-S., 1899.

OSSIFICATION

The degenerated vitreous, or rather the inflammatory connective tissue which replaces the vitreous, may be found ossified in cases of phthisis bulbi, etc., in which the choroid is ossified (*see* Vol. I, Figs. 249, 250, 251, 252, 253). Several cases of primary ossification of the vitreous have been described (Sprée, Wittich, Virchow) in horses and rarely in man (Poncet, Antonelli, Berger). None of these cases is beyond dispute, and probably all were secondary.

SPRÉE.—Ann. d'Oc., xiv, 1845. VIRCHOW.—Die krankh. Geschwülste, ii. WITTICH.—Virchow's Archiv, v. PONCET.—In de Wecker and Landolt, Traité, ii, 1886. ANTONELLI.—Ann. di Ott., xx, 1891. BERGER.—In Lagrange, Tumeurs de l'Œil, i, Paris, 1901. RUMSCHEWITSCH.—A. f. A., xlviii, 1903.

CHAPTER IX

THE CHOROID

THE NORMAL CHOROID

THE choroid consists of five principal layers from without in :— (1) the suprachoroid, (2) Haller's layer or the layer of large vessels, (3) Sattler's layer or the layer of medium-sized vessels, (4) the chorio-capillaris or layer of capillaries, (5) the membrane of Bruch or lamina vitrea. It is bounded on the outer side by the lamina fusca of the sclerotic and on the inner by the pigment epithelium of the retina.

The *lamina suprachoroidea* is composed of thin membranes pervaded by fine elastic fibres and covered by endothelial cells (Schwalbe). It also contains large flattened pigment-cells dispersed irregularly or arranged in patches. Seen on the flat, these cells have many irregular processes, and the pigment consists of round or oval granules. Wandering cells are also present. The layer is loosely attached to the lamina fusca by vessels and bands of connective tissue containing pigment-cells, which are often continued along the vessels as they pierce the sclerotic. There is a lymph space, the *suprachoroidal lymph space*, between the suprachoroid and the sclerotic, and this communicates along the vessels and nerves with the capsule of Tenon (Schwalbe).

Haller's layer consists chiefly of large veins, held together by connective tissue with elastic fibres and pigment-cells like the suprachoroid, but the cells are always branched, which is not invariably the case in the suprachoroid.

Between Haller's and Sattler's layers is an *intermediate layer* representing the *tapetum* of lower animals. It consists chiefly of elastic fibres, thus most closely resembling the tapetum fibrosum, though in quite rudimentary form. On the inner side it is covered with endothelial cells, thus recalling also the tapetum cellulosum of some mammals and fishes.

Sattler's layer consists of medium-sized vessels lying in a fine elastic network with few pigmented cells. In addition to the endothelial covering on its outer side already mentioned it is also covered by endothelial cells on the inner side. The veins, like those of the pia mater, have no muscular tissue; they are enclosed in an adventitia, which is separated from the endothelial interna by a perivascular lymph

space, communicating directly with the intercapillary spaces of the chorio-capillaris. The arteries have a tunica media composed of



FIG. 324.—MEMBRANE OF BRUCH. $\times 200$.

Coats, R. L. O. H. Rep., xvi. Stained with hæmatoxylin and eosin: it is granular, but shows no division into layers.

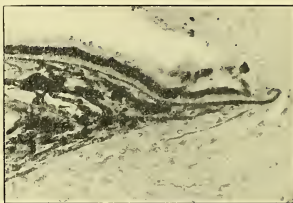


FIG. 325.—MEMBRANE OF BRUCH. $\times 200$.

Coats, R. L. O. H. Rep., xvi. Termination at optic disc, stained by Weigert's elastic tissue stain. It consists of an inner granular layer, and a thin, deeply stained outer line: the inner layer ends level with the pigment epithelium; the outer projects into the substance of the papilla and terminates in an upturned end.



FIG. 326.—MEMBRANE OF BRUCH. $\times 90$.

Coats, R. L. O. H. Rep., xvi. Separation of the two layers over a sarcoma (see Nettleship, T. O. S., xxiv). Near c, a "colloid body," they are normally situated. At A, the outer elastic layer ceases, reappearing as a zig-zag line, but finally ending at B. The inner homogeneous layer, D, passes on, carrying the pigment epithelium and "colloid bodies."

circular muscle-fibres, and there are longitudinal fibres in the tunica adventitia. They also have perivascular lymph spaces. The peri-

vascular lymph spaces are said not to communicate with those present between the planes of the supporting connective tissue.

The *chorio-capillaris* (tunica Ruyschiana) is a network of capillaries, the meshes of which are finest at the posterior pole, and are wider and more elongated near the ora serrata. There are no pigmented cells in this layer. The chorio-capillaris does not extend forwards into the ciliary body.

The *membrane of Bruch* is a homogeneous layer, which stains feebly and diffusely with elastic tissue stains. It is probably the product of secretion of the retinal pigment epithelium (Treacher Collins), and if so, really forms part of the retina. Beneath it is a fine elastic network, *stratum elasticum suprapapillare* (Smirnow). The lamina vitrea is sometimes described as consisting of two layers, an outer elastic and an inner homogeneous. The latter may show fine longitudinal fibrillation. The membrane is thickest near the optic disc, especially the elastic layer, which often curves round the end of the inner layer here (see also "Colloid Bodies").

BRUCH.—Untersuchungen z. Kenntniss des körnigen Pigments, Zürich, 1844. SCHWALBE.—Anatomie des Sinnesorgane, Erlangen, 1885. SÄTTLER. A. f. O., xxii, 2, 1876; C. f. A., i, 1876. SMIRNOW.—A. f. O., xlvii, 3, 1899. SAGAGUCHI.—K. M. f. A., xl, 1902. MÜNCH.—Z. f. A., xii, 1904.

WOUNDS AND INJURIES

The early stages of rupture of the choroid have not been examined microscopically. In direct wounds, caused experimentally or by foreign bodies, other structures are invariably injured in addition. In experimental wounds in rabbits Tepljaschin found the changes to be essentially inflammatory and reparative. The tissues were separated by serous exudate and infiltrated by wandering cells, whilst karyokinetic figures formed a distinct feature in vertical sections. They were principally "internal to the chorio-capillaris," in the layer described as the musculus chorioideæ in rabbits by Hållsten and Tigerstedt. Karyokinetic figures were also seen in the cells of the muscular layer of the walls of the large choroidal vessels. I have found similar results in experimental injuries in monkeys, and it is to be noted that the choroid affords the chief means of repair in these cases, as might be expected from its highly vascular nature. (See "Wounds and Injuries of the Retina").

The same changes are found in cases of injury by foreign bodies as in experimental injuries, but here the question of septic infection arises. When this occurs the tendency to repair varies inversely with the virulence of the infection, other things being equal. Aseptic foreign bodies may become encapsuled, granulation tissue growing round them and subsequently organising into dense fibrous tissue. The granulation tissue often contains foreign-body giant cells, situated, not only in the immediate vicinity of the foreign body, but also at some distance from it. They are never found in cases of metallic splinters.

TEPLJASCHIN.—A. f. A., xxviii, 1894. PARSONS.—R. L. O. H. Rep., xv, 1903.

INFLAMMATION

ACUTE AND SUPPURATIVE

Suppurative choroiditis is usually part of general panophthalmitis, due to a perforating wound with a septic instrument or foreign body; less commonly it is due to endogenous infection (*metastatic choroiditis*), forming part of a general pyæmia.

In both forms the intensity of the reaction depends upon the virulence of the infecting organisms. Infiltration with polymorphonuclear leucocytes occurs first in the inner layers, around the medium-sized and smaller vessels. In perforating wounds, etc., the inflammation is transmitted from the retina (Schöbl, Ruge). The intercapillary sub-



FIG. 327.—PANOPHTHALMITIS. $\times 60$.

From the same specimen as Fig. 193, Vol. I. Note the congestion and infiltration of the choroid and retina, also the perivascular infiltration in the retina.

stance, normally free from wandering cells (Sattler), becomes pervaded with leucocytes, which are, however, still more numerous around the venules and arterioles (Fig. 327). The layer of larger vessels long remains free from infiltration, and this applies even more to the non-vascular supra-choroidea. All the blood-vessels are distended, especially the veins; they contain red corpuscles, together with an excess of leucocytes. The latter are often aggregated at the periphery, adhering to the walls. In some cases the infiltration is limited to the medium-sized vessels, probably owing to the endothelial layers which separate this layer from the choriocapillaris and Haller's layer (Sattler). The hyperæmia, œdema, and infiltration lead to great swelling of the choroid, which may be seven or eight times thicker than normal.

The vessels, besides being distended, are much altered, especially the arteries. The walls are infiltrated, especially the adventitia; the media is often obscured, so that it is impossible to distinguish arteries from veins. The endothelium becomes swollen and desquamated, but the remnants may proliferate later in the more chronic cases, and lead to endarteritis obliterans. The lumen is often filled with a thrombus, composed of fibrin, leucocytes, and a few red corpuscles. The whole wall may be swollen and homogeneous, and necrotic changes rapidly set in. These lead to hæmorrhages, which are usually small and localised, but may be extensive.

Pari passu with the degenerative changes there is usually some evidence of repair, most obvious in the cells of adventitia. In the fulminating cases, due to virulent infection, few or no signs of proliferation are seen. In less acute cases spindle cells are seen streaming out into the surrounding stroma.

The stroma cells become more rounded, their processes being retracted or even broken off. There is little evidence that they proliferate, though binuclear cells are sometimes seen (Knapp). In severe cases they necrose, their nuclei cease to stain, and they finally disappear entirely.

The membrane of Bruch long remains intact, and apparently offers considerable resistance to the fluid exudate, which, although present in considerable quantity in the stroma, is mostly pressed out into the supra-choroidal space. The laminæ here are forced apart, the concentric ones being most resistant, and the choroid is more or less raised from the sclerotic. Some of the fluid filters through the membrane of Bruch, raising the retina, usually only slightly over a large area; occasionally there is a considerable detachment of the retina, more or less localised. Finally, the membrane of Bruch gives way in one or more places; this occurs earlier the more localised the infiltration.

The pigment epithelium of the retina undergoes marked changes. The cells lose much of their pigment, and become swollen and rounded. Many are cast off into the subretinal exudate. The pigment floats free, and much of it is taken up by leucocytes.

The leucocytes are almost entirely polymorphonuclears; they undergo the changes—fatty degeneration, etc.—common to all suppurative conditions.

In panophthalmitis resulting from septic perforating wounds the choroid is affected secondarily to the retina, and may be almost normal. In two situations, near the ora serrata and around the optic disc, it is always inflamed. Anteriorly this is due to direct transmission from the ciliary body; behind the ora serrata the true retina protects the choroid, as is especially well seen when the retina is detached. Posteriorly the inflammation is directly transferred from the head of the optic nerve, which is always early affected, *viâ* the vitreous, in panophthalmitis: the anastomosis of blood-vessels at the disc facilitates the transference. The condition of the other parts of the choroid depends chiefly upon that of the retina. It may be normal if the retina has early become detached, though even in this case there is often slight diffuse infiltration. On the other hand, the choroid may

also remain normal when the acutely inflamed retina is still *in situ*. As a rule, however, in these cases the choroid suffers with the retina, and the most infiltrated parts of the former correspond with the most inflamed parts of the latter. This is very marked when the retina is necrotic, the choroid being usually in the same condition. Besides these methods of infection of the choroid it may also be attacked by way of the suprachoroidal space, *i.e.* from outside. This is due to filtration of toxins, etc., from the ciliary body into the space, where they may cause localised foci, or may become diffused and lead to general choroiditis.

Suppurative choroiditis may in rare cases be due to extension along the perforating vessels from Tenon's capsule (Hodges).

Metastatic suppurative choroiditis is a comparatively rarely observed phenomenon, possibly owing to the gravity of the cases in which it might be expected to occur. It is found particularly in septic puerperal cases, as well as in surgical pyæmia, and after acute infectious diseases. It was first investigated by Meckel and Müller, later by Virchow, Roth, Litten, Heiberg, Hirschberg and others. It is usually due to streptococci, more rarely to staphylococci or pneumococci; the intensity of the virulence diminishes in the order named (Axenfeld). The organisms form emboli in the small vessels or capillaries, or escape from them into the surrounding tissues. Since the retinal capillaries are much narrower than the choroidal ($5-6 \mu$: $10-30 \mu$) the retina is generally first attacked. When clinical grounds render primary affection of the choroid probable, it usually starts in the anterior part where the capillaries are narrowest (Axenfeld). In most cases both membranes are involved, and it is impossible to decide the primary site.

It is often impossible to demonstrate the organisms after death, as they usually disappear rapidly. When found they are most numerous, not in the choroid, but between the pigment epithelial cells, in the retina, and in the vitreous, especially in the pus. Herrnheiser found the choroidal vessels full of streptococci, whilst the surrounding tissues were quite normal; this can only have been due to multiplication shortly before or after death, when inflammatory reaction was no longer possible.

Metastatic choroiditis occurring during the puerperium usually ends in panophthalmitis, followed by perforation, rarely in phthisis bulbi without perforation. The latter seems to be somewhat commoner during surgical pyæmia.

KNAPP.—A. f. O., xiii, 1, 1867. SATTLE.—A. f. O., xxii, 2, 1876. MECKEL.—Annalen der Charité, v, 1854. MÜLLER (1857).—Gesammelte Schriften, Leipzig, 1872. VIRCHOW.—Virchow's Archiv, x. ROTH.—Deutsche Zeit. f. Chirurgie, 1872. LITTEN.—Berliner klin. Woch., 1878; Zeit. f. klin. Med., 1881. HEIBERG.—Centralbl. f. med. Wissenschaft, 1872. HIRSCHBERG.—A. f. A., viii, 1879. KAHLER.—Zeit. f. Heilkunde, i, 1880. SCHÖBL.—A. f. A., xxi, 1890. VOSSIUS.—Zeit. f. Geburtshilfe u. Gynäkologie, xviii, 1890. HODGES.—Ophth. Rev., ix, 1890. HERRNHEISER.—Zeit. f. Heilkunde, xiv, 1893; K. M. f. A., xxxii, 1894. AXENFELD.—A. f. O., xl, 4, 1894. GOH.—A. f. O., xliii, 1, 1897. TERRIEN.—A. d'O., xix, 1899. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. WAGENMANN.—A. f. O., xxxiii, 2, 1887. BULL.—T. Amer. O. S., 1901. BIETTI.—Ann. di Ott., xxxii, 1903. STOCK, LIEBRECHT.—K. M. f. A., xli, 1903. SELENKOWSKY AND WOJECZOWSKY.—A. f. A., xlvii, 1903. RUGE.—A. f. O., lvii, 3, 1904. *FUCHS.—A. f. O., lviii, 3, 1904.

SUBACUTE AND CHRONIC CHOROIDITIS

Non-suppurative choroiditis—*Choroiditis exudativa*—is subacute or chronic in its course. It shows a variety of forms, all having a fundamental resemblance, but differing widely in details. It is distinguished by vascular congestion, infiltration with leucocytes, chiefly mononuclears, and œdema. The changes are usually localised, with numerous foci, but may also be diffuse; the fluid exudate may be slight, or it may be so great as to lead to distension of the suprachoroidal space, and even widespread detachment of the retina. The causes of these varieties are by no means fully understood, but their association with definite clinical types is in some cases well established. The earliest stages, which might be expected to afford the most valuable information, have seldom been observed anatomically.

Considering first the common fundamental characteristics, the most striking feature is the infiltration with lymphocytes. This may be localised (*nodular choroiditis*), especially around some of the distended vessels of Sattler's layer, or it may be diffuse. In the latter case it is often confined at first to the neighbourhood of the choriocapillaris, but it is frequently most evident in the middle or outer layers. Besides the lymphocytes, the mast cells are also increased.

The blood-vessels are dilated, especially in the areas of infiltration; they often contain an abnormal number of leucocytes, chiefly arranged at the periphery. The endothelial cells of the capillaries are often much swollen, so that they project into the lumen. This is best seen in flat preparations (Ginsberg).

The stroma-cells are only seen with difficulty, being obscured by the lymphocytes. In the less infiltrated parts they are found to be rounded, with their processes retracted. The chromatophores are aggregated around the nodules, and are also found in the superficial layers, where they are normally absent; hence it would appear that they are capable of wandering, whereas there is little evidence of their proliferation, at any rate in the earlier stages. Many undoubtedly undergo degenerative changes, becoming clumped together so that they resemble pigment epithelial cells. Others break up, setting free their pigment, which is largely taken up by leucocytes. Extensive necrosis is never found except in tubercular or syphilitic cases, though caseation has been described when these ætiological factors could not be proved (Wedl and Bock, Friedland).

The pigment epithelium of the retina undergoes degenerative changes, especially in those cases in which the inner layers of the choroid are most affected, and above all when the membrane of Bruch has been broken through. The cells become œdematous and swollen, loosened from their attachments, and finally shed. Many break down, setting free their pigment, much of which is taken up by leucocytes. Others are stimulated to proliferate, which they do in an apparently aimless manner, becoming heaped up in the subretinal space. The young cells are at first round, with round or oval nuclei, and are devoid of pigment; according to Krückmann, only these young cells are actively amœboid. In any case, many retinal pigment cells find their

way into the retina proper, which always undergoes more or less degeneration, suffering from the interference with the choroidal blood-supply, upon which the outer layers of the retina are dependent for nutrition. When the membrane of Bruch is broken retinal pigment cells penetrate the stroma of the choroid, though here they are distinguished with difficulty from the metamorphosed chromatophores. The free pigment is also taken up by the endothelium of the vessel walls, and the migrant pigment cells show a marked tendency to congregate around the vessels, especially in the retina; the picture of retinitis pigmentosa is thus very accurately simulated. Krückmann states that the proliferating cells often assume the spindle shape, forming laminae which are only to be distinguished from fibrous tissue by the absence of vessels; it is probable, however, that in most cases these spindle cells are of different, mesoblastic, origin.

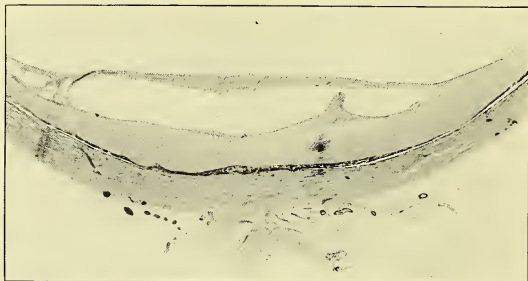


FIG. 328.—FIBROUS TISSUE ON THE CHOROID. $\times 8$.

From a woman, æt. 49; eye blind thirty years. Almost complete fibrous degeneration of the retina, with partial detachment. Thick layer (1 mm.) of hyaline fibrous tissue, with calcareous spots, on surface of choroid; choroid degenerated, membrane of Bruch only visible in places under fibrous mass.

The chronic inflammatory process passes insensibly into one of cicatrisation, the amount of scar tissue formed varying enormously in different cases. Even in the later stages of traumatic suppurative inflammation the regenerative process goes on simultaneously with the destructive (see "Wounds of the Retina"). In subacute and chronic choroiditis the formation of granulation tissue early becomes a prominent feature, and may be very extensive, involving, not only the choroid, but also the retina, and even the vitreous (*choroiditis hyperplastica*, Schöbl). The granulation tissue later is transformed into dense fibrous tissue in the usual manner. In most cases, however, the cicatricial process is moderate in extent, going on *pari passu* with the fibrous degeneration of the retina; eventually both membranes are fused together into a firm scar. As the new connective-tissue cells are formed in the choroid the lymphocytes recede before them and very

gradually dwindle, some being destroyed, whilst probably the majority pass back into the lymph-stream. This process is in most cases an extremely slow one, and nodules of lymphocytes may be seen, encap-



FIG. 329.—CONNECTIVE TISSUE ON THE CHOROID. $\times 9$.

The lenticular mass of tissue lying upon the choroid is largely composed of layers of endothelial cells; it is infiltrated at the periphery with polymorphonuclear leucocytes. Right eye, blind thirty-five years, of a woman *æt.* 45.

suled, as it were, in fibrous tissue, many months after the onset of the disease.

The granulation tissue is not limited to the choroid, from which it

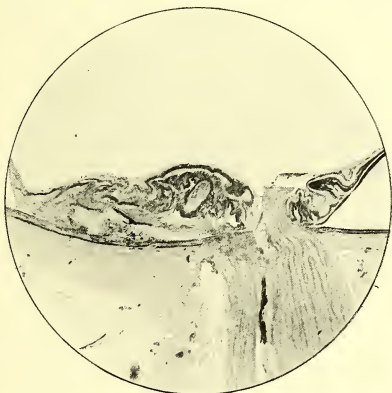


FIG. 330.—FOLDING OF THE RETINA. $\times 10\cdot5$.

From a boy, *æt.* 8½ (see Paton, T.O.S., xxiii, 1903; Parsons, T. O. S., xxiv, 1904). Folding produced by contraction of fibrous tissue laid down by choroid.

springs: it passes through the apertures in Bruch's membrane and invades the subretinal space, spreading along the surface of the choroid (Figs. 328, 329). Here it comes into direct contact with the retinal

pigment epithelium, which, like the epithelium of a granulating wound, invades every available nook and crevice. Hence arise plugs and islets of epithelium, and spaces and tubules lined with epithelium. As the tissue organises many of these are throttled out of existence; others remain only as grotesquely shaped masses and strands of pigment. The changes undergone by the retinal pigment epithelium in these and analogous conditions have been exhaustively investigated by Krückmann.

The contraction of the organising connective tissue often leads to puckering and folding of the retina, which may ophthalmoscopically simulate a tumour (Paton, Parsons) (Fig. 330).

The organisation of the granulation tissue in the choroid itself involves the destruction of the normal blood-vessels. This occurs partly as the result of obliterating endovascular changes, but chiefly from the



FIG. 331.—FOLDING OF THE RETINÄ. $\times 55$.

Showing fibrous tissue and pigment proliferation, with folding of the retina caused by contraction of the fibrous tissue.

constricting effect of the contracting fibrous strands. Finally few or no blood-channels can be seen in the dense scar, though a few of the larger vessels may survive, being greatly distended owing to the unequal pressure.

The scar tissue readily undergoes degenerative changes; the nuclei diminish in numbers, the fibres are pressed closer together, often becoming hyaline. The whole choroid at the sites affected may thus become transformed into masses of hyaline tissue, with scanty nuclei and patches of retained pigment. Indeed, the new tissue frequently transgresses the limits of the choroid, invading the subretinal and sub-choroidal spaces. In this manner patches of simple atrophy and of hyperplastic scar tissue often lie side by side.

The degenerative changes go even farther, the tissue becoming calcified, and finally ossified by the agency of osteoblasts derived from the choroid (see "Ossification of the Choroid").

Not only is fibrous tissue formed upon the inner surface of the choroid and in its substance: it may also be formed upon its outer surface, replacing the suprachoroidea by dense scar tissue (Fig. 332). It has already been pointed out how the choroid may be attacked by inflammation from the outer side (*v. p. 448*). The suprachoroidal space then at first contains exudates, which correspond in situation with foci of inflammation in the overlying uvea; the space outside the flat part of the ciliary body is usually first affected. In the milder attacks of exogenous and endogenous inflammation these exudates organise; such a case was first described by Schiess (-Gemuseus). The same condition



FIG. 332.—SUPRACHOROIDITIS. $\times 55$.

From a specimen by Professor Wintersteiner; an eye with traumatic iridocyclitis. There is a thick layer of dense fibrous tissue, poor in cells, lying on the outer side of the choroid, possibly due to organisation of blood-clot.

may ensue from subchoroidal hæmorrhage (Bloom). It is by no means an uncommon feature in shrinking or shrunken eyes. The chromatophores of the suprachoroidea undergo the usual inflammatory changes; they lose their processes and become rounded, the pigment being aggregated into large dense clumps. The leucocytes and blood-corpuses gradually disappear. The chief changes are seen in the endothelial cells. These normally show only large pale nuclei, crossed by elastic fibres of the suprachoroidea. They now show a definite cell body with processes (Fuchs). These form a network, or run parallel to each other, the intercellular substance showing fine fibrillæ. In van Gieson specimens the new tissue is red and clearly distinguished from the original suprachoroidal stroma. The fibrillæ increase in

numbers, and are orientated like the original planes of the suprachoroidal laminæ, being subjected to similar stress and strain. The fibrillæ develop into thicker fibres, and the nuclei become longer, narrower, and more deeply stained. The new fibrous tissue is especially noticeable around the blood-vessels, showing the important part played by the adventitia in its production. The fibres often form a thick network with few nuclei; in other places they run parallel, following the direction of the choroid and sclera. The suprachoroidal lamellæ are gradually replaced by this thick tissue, but are long recognisable as strands of pigment cells.

The thickened suprachoroidal tissue is traversed by new-formed vessels, which greatly vary in number. Their development from simple endothelial tubules to fully-formed vessels, sometimes going on to hyaline degeneration, can be well traced. Most are derived from the anterior and posterior ciliary arteries, but some grow direct from the scleral vessels.

The new tissue often contains spaces of various sizes, due to collections of fluid exudate. As the droplets increase in size the pigment and endothelial cells are pushed aside, so that large, round, or elliptical spaces are formed. The larger the spaces, the more densely is the fibrous tissue pressed together, and the wall is further thickened by proliferation. The thickening is generally seen first at the posterior end of the larger spaces, filling in the triangular space between the detached choroid and the sclera; later it becomes evident at the anterior end, and finally a dense capsule is completely formed. The inner surface of the capsule is smooth, and often has a sort of endothelial lining, as shown by the flattened nuclei.

The thickest suprachoroidal membranes are found after hæmorrhage, but there is good evidence that they also occur with simple serous exudation. They become denser, less nucleated, and poorer in blood-vessels as they grow older. They are particularly free from vessels when they are adherent to the sclerotic, whilst those adherent to the choroid may be extremely vascular. Often the membrane is fused neither with the choroid nor the sclerotic, but is separated from both by layers of spongy lamellæ; this corresponds with the distribution of the exudate in many early cases of inflammation. The choroid may be thrown into large folds by the contraction of the organising tissue. The membranes adherent to the sclera are commoner than the other types; the limitation from the sclera is always well marked, since the tissue is always richer in nuclei, and is more finely fibrillated.

The masses of fibrous tissue may be several millimetres thick, so that it is not surprising that such a case has been described as a fibroma of the choroid (Schiess). They apparently never, in their later stages, undergo ossification (Fuchs), therein differing in a striking manner from the similar deposits on the inner surface of the choroid.

The inflammatory process is accompanied by increased secretion from the choroid. This is at first slight, and in many types of sub-acute choroiditis remains so permanently. It is then limited to an œdematous condition, with some accumulation of fluid in the sub-choroidal spaces. The secretion rapidly becomes pathological as regards its constituents, containing, like all inflammatory secretions,

an excess of proteids, which are allowed to filter through the injured vessel walls. The pathological exudate, like its normal progenitor, filters through the membrane of Bruch into the retina, and even through this into the vitreous. The cellular—leucocytic—and probably the precipitated albuminous constituents thus give rise to the dusty or more concrete opacities in the vitreous which are familiar in the ophthalmoscopic picture. In the more severe cases the ciliary body undoubtedly participates in the inflammation, especially in anterior choroiditis, and it is improbable that the grosser opacities can be formed without such participation. We are more cognisant of the liability of the ciliary body to participate with the iris in inflammatory processes, because here they are more readily observed. The uveal tract, however, in many diseases suffers as a whole, as might be expected on anatomical and physiological grounds. It is more than probable that the part played by the ciliary body in many forms of choroiditis has hitherto been under-estimated.

In the well-known clinical types of choroiditis the amount of fluid exudate is small; it is rarely sufficient to cause marked swelling or raising of the retina. In hardened and dehydrated preparations the swelling is even less noticeable, but the former presence of exudate can be seen in the finely granular deposits of coagulated albumen. Occasionally fibrinous coagula are found in or upon one or other surface of the choroid. Rarely the amount of exudate is sufficient to cause local detachment of the choroid or retina. Similar deposits are found as a *post-mortem* change, but here the general distribution will usually prevent mistake.

There is, however, a more generalised inflammation, chiefly affecting the choroid, which is usually included under the term "choroiditis exudativa," and is regarded wrongly by some as a form of suppurative choroiditis. The commonest type of *pseudoglioma* belongs to this category. Here, usually as the result of some acute infectious disease in children, a chronic uveitis is set up which causes detachment of the retina, and finally phthisis bulbi (Fig. 333). Allied cases are more rarely seen in adults. It is probable that here there is no direct attack upon the uveal tract by pathogenic organisms, though this is by no means disproved, but that the inflammation is set up by the action of toxins circulating in the blood. In any case the organisms or their toxins are not pyogenic, and it is therefore wrong to include the condition amongst the purulent inflammations.

Treacher Collins, who has been able to examine some early cases of *pseudoglioma* (four days and two weeks), thinks that it commences as a retinitis. He says that the exudation from the retinal vessels passes into the vitreous, the hyaloid membrane becoming adherent to the inner surface of the retina. The pars ciliaris retinæ is usually soon involved, whilst later inflammation extends to the stroma of the ciliary body and iris, nodules of round cells accumulating in them. Occasionally neither the iris nor ciliary body becomes at all affected. The choroid more often escapes than the anterior portions of the uveal tract; when it is implicated the part bordering on the optic nerve is most often inflamed. There is nearly always marked proliferation of the epithelial cells on its inner surface: some of them grow into the

substance of the retina, and patches may remain adherent to its outer surface when it has become detached. These proliferated epithelial pigment-cells seem to give rise subsequently to hyaline deposits, or to undergo fatty degeneration, crystals of cholesterin forming amongst them. In the later stages the conditions are those of a plastic cyclitis—cyclitic membranes and deposits, ingrowth of pigmented tubules from the pars ciliaris, retraction of the periphery of the iris, etc. It is important that further observations on early cases should be recorded, for

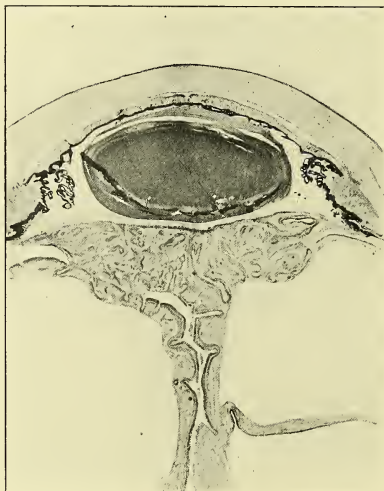


FIG. 333.—PSEUDOGLIOMA. $\times 8$.

From a girl, *æ*t. 6. Note absence of a. c., presence of broad, shallow anterior capsular cataract of inflammatory origin, thin cyclitic membrane behind lens, and complete detachment with folding of the retina.

there can be no doubt that the later stages point rather to a primary cyclitis than to a retinitis.

Although this condition is not a pure choroiditis, it may be conveniently discussed here. It differs from suppurative choroiditis, as has been already mentioned, in the fact that no pus is formed, and it differs from the ordinary types of subacute and chronic choroiditis in that large quantities of fluid exudate are poured out to fill up the large subretinal space. The exudate differs in no respect from that invariably found beneath a retina detached from any cause. It will be best to

leave the discussion of its production to another place; its nature and the changes which it undergoes will alone be considered here.

The exudate is fluid in the fresh state, but becomes transformed into a transparent jelly after hardening in formol. It is usually greenish in colour, owing to altered blood-pigment, and often contains glittering particles—cholesterin crystals. If the fresh or formol-treated exudate is examined under the microscope before treating with alcohol or ether, the cholesterin crystals are recognised by their very characteristic shape of notched rhombic plates. They may also be subjected to the usual chemical tests. Cholesterin ($C_{27}H_{45}.OH$), an alcohol, gives the following colour reactions:

(1) With iodine and concentrated sulphuric acid the crystals give a play of blue, red, and green, finally dissolving.



FIG. 334.—GIANT CELLS IN THE RETINA. $\times 120$.

From a boy, *æt.* 4, with iridocyclitis. The periphery of the iris was retracted, and the retina was detached anteriorly. Lying in and upon the inner surface of the retina were numerous groups of giant-cells, arranged around cholesterin crystals. The space from which a cholesterin crystal has dissolved out is seen in the upper part of the figure.

(2) Heated with sulphuric acid and water (5:1) the edges of the crystals turn red. These tests are best performed under the microscope.

(3) A solution of cholesterin in chloroform shaken with an equal amount of concentrated sulphuric acid turns red, and ultimately purple, the subjacent acid acquiring a green fluorescence (Salkowski).

In sections the cholesterin is no longer seen, having been dissolved out by the alcohol and ether, but the spaces from which the crystals have disappeared are easily recognised; these are nearly always long slits in the granular *débris*, since the spaces are rarely cut on the flat. (Fig. 334).

Besides cholesterin the granular *débris*, consisting of coagulated albumen with free pigment granules, contains cells. Most of these are leucocytes undergoing degenerative changes. Some are slightly swollen, but retain well-stained nuclei; the cytoplasm often contains pigment granules. Others are more swollen, and have shrunken nuclei. Others are little more than a network of protoplasm, marked out by pigment; they then have a mulberry-like appearance. Others, finally, are mere ghosts of cells. Free pigment epithelial cells are also seen, generally swollen and degenerated, and containing fatty globules, which are also found in the leucocytes. The fat is dissolved out by ether, but the round vacuoles show where it previously existed. Almost invariably there are many red corpuscles, isolated or in rouleaux.

The denser exudate has a tendency to adhere to the tissues, especially to the outer surface of the detached retina (Greeff). The cholesterin acts like a foreign body, irritating the tissues, so that giant cells are often formed around the crystals; in this manner the crystals frequently lie imbedded in giant cells, and indeed within the cells themselves (Fig. 334). Thus masses of exudate, cholesterin, giant cells, pigment cells, leucocytes, etc., lie upon and even in the retina and choroid, both of these structures being in an advanced state of degeneration or atrophy. The masses of exudate may become encapsuled or organised, so that tumour-like excrescences occur upon the retina or, less commonly, the choroid. These appear as dense cicatricial fibrous tissue, with scanty nuclei, a few vessels, and the scattered constituents of the exudate. Such masses may even occur in the substance of the choroid (Cramer and Schultze).

H. MÜLLER.—A. f. O., iv, 1, 1858. RAAB.—A. f. O., xxiv, 3, 1878. SCHIESS (-GEMÜSEUS).—Virchow's Archiv, xlv. NORDENSON.—Die Netzhautablösung, Wiesbaden, 1887. LAW-FORD.—T. O. S., viii, 1888. SCHÖBL.—A. f. A., xx, 1889; xxi, 1890. TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1892. AXENFELD.—A. f. O., xl, 4, 1894. CRAMER AND SCHULTZE. A. f. A., xxix, 1894. GREEFF.—Berl. klin. Wochenschrift, 1897. BLOOM.—A. f. O., xlv, 1, 1898. FRIEDLAND.—A. f. O., xlviii, 2, 1899. KRÜCKMANN.—A. f. O., xlviii, 2, 1899. PATON.—T. O. S., xxiii, 1903. PARSONS.—T. O. S., xxiv, 1904; xxv, 1905. FUCHS.—A. f. O., lviii, 3, 1904.

CHOROIDITIS DISSEMINATA

Typical choroiditis disseminata, so called from the ophthalmoscopic appearances, has seldom been examined microscopically (Schweigger, Iwanoff, Pagenstecher, de Wecker). The changes are those already described for chronic choroiditis. There is at first a circumscribed perivascular infiltration in the innermost layers of the choroid, and the outer layers may remain quite normal (Pagenstecher) (Fig. 335). The infiltration increases, causing slight swelling; this stage corresponds with the yellow spots seen with the ophthalmoscope. The membrane of Bruch may remain intact, but exudation collects in small quantity between the retina and choroid. The pigment epithelium suffers from malnutrition, undergoing the changes already described (p. 449). The infiltration area becomes organised, the vessels being destroyed by the process; the retina invariably becomes degenerated over the spot, and is knit together with the choroid by means of fibrous tissue (Fig. 336). According to Murakami the fibrous tissue is chiefly neuroglia, derived

from the retina, and invading the choroid ; it stains orange-yellow with van Gieson, whilst the choroidal stroma stains rose-red. Such minutiae

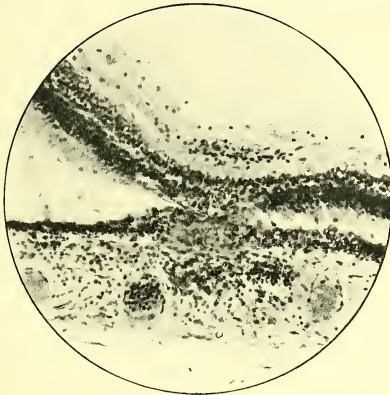


FIG. 335.—CHOROIDITIS DISSEMINATA SYPHILITICA. $\times 120$.

From a specimen by Professor Wintersteiner, showing a very early patch. Note the proliferation of the cells through the lamina vitrea.



FIG. 336.—CHOROIDITIS DISSEMINATA SYPHILITICA. $\times 60$.

From the same specimen, showing adhesion of retina to choroid.

of differential staining are not sufficient to prove the point, and it is more probable that the fibrous tissue is mesoblastic—derived from the

choroid, and in small degree from the retinal vessel walls. The amount of fibrous tissue formed is generally very small; indeed, the retina and choroid are usually thinned and atrophic. The more fluid exudate tends to collect around the affected spot, so that the retina here is slightly raised from the choroid. The pigment disappears from the centre of the affected area, but collects at the edges, where it is often very dense, thus accounting for the ophthalmoscopic picture. After the retina has degenerated, and not until then, pigment may invade this structure (*v. infra*).

Stock has obtained rarely a metastatic disseminated choroiditis in rabbits by the intravenous injection of cultures of *Bacillus pyocyaneus* β .

SCHWEIGER.—A. f. O., ix, 1, 1863. IWANOFF.—K. M. f. A., vii, 1869. PAGENSTECHER.—A. f. O., xvii, 2, 1871. SCHÖN.—K. M. f. A., xiii, 1875. DE WECKER.—In G.-S., iv, 1876. *MURAKAMI.—A. f. O., liii, 3, 1902. STOCK.—K. M. f. A., xli, 1903.

SYMPATHETIC CHOROIDITIS

The changes found in the choroid in sympathetic ophthalmia are essentially those of chronic choroiditis, but they sometimes show characteristic differences. The same changes have been observed in the few cases in which the sympathising eye has been examined.

In the first stage nodules of infiltration (*nodular choroiditis*) are found around the vessels of the outer layers, the choriocapillaris remaining free, the condition differing in this respect from disseminated choroiditis. In the second stage the infiltration becomes more diffuse, and all the phenomena of chronic choroiditis are seen—infiltration with leucocytes, increase of mast cells, degeneration and heaping up of chromatophores, sclerosis of the vessels, etc. There is a marked tendency, however, to unusual endothelial proliferation and the formation of giant-cells, which are especially found in the neighbourhood of the larger vessels (Schirmer). The histological appearances thus much resemble tubercle (Krause, Axenfeld, Uhr, Peters). They differ in the relationship of the giant cells to the vessels, most being associated with the arteries, and seeming to spring from the endothelium of the adventitia (Axenfeld, Uhr); moreover, the lumen of the vessel is often intact. They further differ in the absence of characteristic tubercle systems, with giant cells in the centre, surrounded by epithelioid cells, and also in the absence of caseation and tubercle bacilli. The areas with giant cells lie imbedded in diffuse round-celled infiltration; they may be distinguished, even under low magnification, by their paler colour (Krause). Exudates early collect in the supra-choroidal spaces, so that the choroid may be slightly detached; they show a great tendency to coagulate with the formation of fibrinous coagula. These also occur on the surface of the pigment epithelium, later shrinking and becoming organised. In the final stages the epithelioid cells are scanty and no giant cells are found (Schirmer).

KRAUSE.—A. f. A., x, 1881. AXENFELD.—B. d. o. G., 1897; K. M. f. A., xxxviii, 1900. UHR.—Inaug. Dissertation, Marburg, 1898. PETERS.—Z. f. A., iii, 1900. *SCHIRMER.—In G.-S., 1900.

SYPHILIS

Syphilis is one of the commonest causes of choroiditis, which generally manifests itself in the disseminated form. In most cases the disease is very chronic, and the changes found anatomically are those already described (pp. 449, 458). It is only necessary here to refer to the information obtained from the scanty records of cases in which the syphilitic element was undoubted.

Choroiditis occurs both in hereditary and in acquired syphilis. The earliest anatomical examination on record is that of a case of interstitial keratitis, with cataract, choroiditis, and iritis, reported by Jonathan Hutchinson (1860). "The stellate pigment of the choroid and the large choroidal vessels offered no peculiarities. Numerous clusters of cells were deposited round the capillaries and round those of the larger choroidal vessels which are near the elastic lamina. . . . Some of the blood-vessels were entirely surrounded by cells, others only on the side nearest the elastic lamina. The latter had in many places disappeared, and the cells had passed through the gaps and occupied the place of the adjoining rods. . . . The hexagonal cells appeared normal, except those over portions of choroid which were occupied by clustered cells, and except those which immediately surrounded the apertures in the elastic lamina. The former had lost their hexagonal shape; they were rounded off, and their pigment granules, instead of being of a pale-brown colour as the remainder, appeared, some deep brown, others black, which, seen with the naked eye, gave the choroid the appearance of being sprinkled with black dots. . . . The clusters of cells were most numerous in the portion of choroid at the equator of the eye; the choroid round the optic nerve and yellow spot appeared healthy."

Nettleship (1886) published an exhaustive investigation of the retina and choroid in several cases of syphilis. He found in the earliest stage nodules of infiltration with small round cells, limited to the choriocapillaris. He described them as gummata, but they differ in no respect from the nodules found in other types of chronic choroiditis; moreover, they show no signs of necrosis, but this is not invariably present in gummata elsewhere. The infiltration shows more tendency to lateral extension than to invasion of the deeper layers, and even in the severest cases the deepest layer, the lamina fusca, was tolerably free. These observations, again, accord with those of some other types of chronic inflammation of the choroid. The same applies to the intra- and supra-choroidal effusions described. Nettleship draws attention to the localised discrete foci in the choroid as compared with the greater generalisation in the retina, where the infiltration is most marked in the nerve-fibre layer.

Later observers have described more advanced cases. Here a diffuse infiltration of the choriocapillaris, followed by invasion of the middle and deeper layers, is superposed upon the nodular choroiditis (Baas), and, indeed, the condition passes on through all the stages already described for chronic choroiditis. Degenerative changes in the vessels may be absent (Edmunds and Brailey) or very slight (Nettleship, Brixia), but, as in most syphilitic conditions, they are generally a prominent feature (*see*

"Degeneration of Vessels"). They are, however, in no respect pathognomonic (Nagel), and there is no evidence that they are always primary.

It will be seen that the changes in nodular and diffuse syphilitic choroiditis are indistinguishable from those due to other causes. More advanced and more complicated cases have been reported, but here there is difficulty in apportioning the ætiological factors. Fialho's is a case in point. The choroid was uniformly infiltrated, but anteriorly and to one side it was enormously thickened. Here there were tubercle-like nodules imbedded in the lymphoid infiltration; they consisted of epithelioid cells with giant cells of the Langhans type in the centre, but there was no necrosis. Anteriorly the ciliary body and iris were changed into granulation tissue. No tubercle bacilli could be found, but the possibility of a mixed infection cannot be eliminated.

True gummata of the choroid, characterised by necrosis, are of extreme rarity; indeed, only gummatous infiltration has hitherto been observed (v. Hippel, Schöbl, Parsons). The changes described above occur in the tertiary stage as well as earlier, but necrosis is absent (*cf.* Vol. I, p. 355). v. Hippel's case was essentially one of gumma of the ciliary body, with diffuse extension into the choroid and other parts of the eye; similar cases have been reported by other observers (*see* "Ciliary Body"). There is dense infiltration with small round cells, with some endothelial proliferation. The granulomatous nature is emphasised by the rich development of new vessels, mostly mere endothelial tubules. The distinctive feature is the fatty degeneration of the tissues, going on to total necrosis. Schöbl has also described thickening of the choroid with nodular infiltration, the largest nodules being in a state of necrosis. Endarteritis was noted, and this may account for the extensive degeneration. I have seen diffuse gummatous infiltration of choroid in a rare case of gumma of the optic nerve (*see* "Gumma of the Optic Nerve").

HUTCHINSON.—R. L. O. H. Rep., ii, 1860. NETTLESHIP.—Trans. Path. Soc., xxviii; R. L. O. H. Rep., vii, 1873; xi, 1886. EDMUNDS AND BRAILEY.—R. L. O. H. Rep., x, 1880. FUCHS.—A. f. O., xxx, 3, 1884. ROCHON-DUVIGNEAUD.—A. d'O., xv, 1895. *BAAS.—A. f. O., xlv, 3, 1897; xlv, 3, 1898. BRIXA.—A. f. O., xlviii, 1, 1899. NAGEL.—A. f. A., xxxvi, 1898. FIALHO.—A. f. O., lii, 3, 1901. V. HIPPEL. A. f. O., xiii, 1, 1867.

TUBERCLE

The first case of tubercle of the choroid was reported by Manz in 1858; he added two others in 1863. Another case was recorded in 1866 by Busch, and the subject was investigated by Cohnheim in 1867. Up to this time affection of the choroid was held to be rare in miliary tuberculosis, but Cohnheim showed that this view was wrong. His observations have been amply confirmed by Brückner, Dinkler, Bock, B. Fränkel, Litten, and others.

Later it became evident that tubercle of the choroid did not necessarily assume the miliary form, but might occur as solitary tubercle or as a simple chronic choroiditis. These forms, too, were considered rare by the earlier observers—v. Graefe, Horner, Neese, and others; but this was disproved by v. Michel and his pupils, Haab, and others.

Tubercular choroiditis may therefore be conveniently described under the designations miliary and chronic.

Miliary Tubercle.—Cohnheim found that the choroid was frequently affected in general miliary tuberculosis; Bock put the percentage at 82·7, Litten at 75. It often occurs only shortly before death.

The number of tubercles varies greatly; there are generally only three or four, but as many as 60 or 70 have been found. Both eyes are usually affected. Any part of the choroid may be attacked, but preference is shown for the neighbourhood of the disc; this may be due, however, to the statistics depending chiefly upon ophthalmoscopic data. The first case described was one in which the tubercles were so far peripheral as to be quite beyond the ophthalmoscopic field of vision, and they are often found in this situation in the *post-mortem* room.

The nodules vary in size from pale pin-point specks to 1 or 2 mm. in diameter (Fig. 337); they may be even larger, but this is unusual,

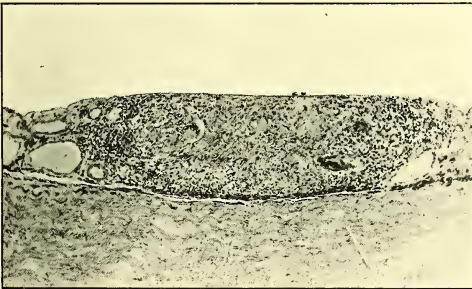


FIG. 337.—TUBERCLE OF THE CHOROID. $\times 60$.

From a child with hip disease who died of meningitis. Note the giant cells, and the round cells at the periphery.

and is due to confluence of smaller ones. They generally project inwards slightly, so as to raise the retina, but the inner surface is often quite flat, whilst the outer surface projects into the sclera.

The smaller nodules may consist only of groups of round cells, as in nodular choroiditis; most, however, have the typical structure of miliary tubercle, consisting of giant cells of the Langhans type, with peripherally situated nuclei, surrounded by epithelioid cells, often having two nuclei, and a peripheral zone of mononuclear leucocytes. The giant cells may contain pigment granules. The centre of the larger tubercles is often caseous. The choroidal stroma disappears inside the nodules, with the exception of occasional patches of pigment. Most of the vessels in the affected area undergo endothelial proliferation and degeneration of their walls, whereby they are finally obliterated. The resulting malnutrition largely accounts for the caseation. The

caseous parts stain only with eosin and diffuse stains, and the degeneration of the neighbouring cells is shown by their nuclei staining badly or not at all. There is frequently a vessel in this situation, as first pointed out by Manz and confirmed long afterwards by Margulies; it is usually a vein. The tubercles may start in any layer of the choroid. Manz described them in the middle layer, developing from the adventitia of the larger vessels, but most of the earlier observers thought that they were commoner in the choriocapillaris (Busch, Cohnheim, Bock). Bock found large tubercles surrounding the large vessels of the outer layer, but considered that they had extended from the choriocapillaris; Dinkler, however, found them developing under the choriocapillaris. Margulies pointed out that the nodules do not necessarily project inwards, but may extend into the suprachoroidea and involve the sclerotic.

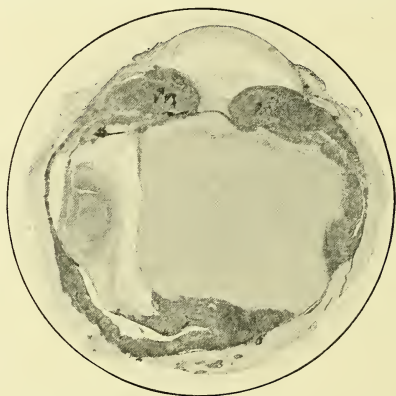


FIG. 338.—TUBERCLE OF THE UVEAL TRACT. $\times 3$.

From a specimen sent by Professor Fuchs. Spontaneous dislocation of the lens.

Here there is frequently a large vessel in the centre, and this probably represents the starting-point and the oldest part, since it is here that necrosis is most marked. Indeed, the nodules show a tendency to follow the tributaries of the vortex veins, and Wedl and Bock figure a flat preparation which illustrates this feature. The relationship to the veins is evidence in favour of infection by way of the lymph rather than the blood-channels, the perivascular lymphatics being the primary seat; probably both methods occur.

The number of tubercle bacilli found varies enormously. They may be apparently absent entirely, or they may be present in very large numbers. Wedl and Bock found them, not only massed in the adventitia of a large vessel, but also within the lumen itself. They are most numerous in the caseous area, and most sparse in the purely lymphoid nodules.

The choroid surrounding the nodules shows little sign of inflammation, perhaps owing to the rapid onset of death. The retina over them is generally normal; Bouchut and Schmidt-Rimpler observed optic neuritis.

Lüttge has described a case of tubercular panophthalmitis occurring during the puerperium.

Chronic tubercle.—v. Michel has advanced the opinion that simple chronic choroiditis may be tubercular in subjects affected with this disease; it may assume all the characteristics of disseminated choroiditis. The evidence in favour of this view cannot be said to be conclusive.

Chronic tubercle of the choroid usually has one of two forms: a



FIG. 339.—TUBERCLE OF THE CHOROID. $\times 120$.

Very widespread tuberculosis of the choroid. Note absence of typical tubercle systems, especially of epithelioid cells.

diffuse inflammation affecting large areas or the whole choroid and characterised by the extensive development of granulation tissue; and the formation of a large circumscribed, tumour-like mass, the solitary or conglomerate tubercle (Wagenmann).

The first form is the commoner; in it the choroid is destroyed and replaced by granulation tissue. Lying in this are ill-defined miliary tubercles, and giant cells are scattered about diffusely or in groups (Fig. 339). The blood-vessels show proliferation of their endothelium and adventitia; large areas undergo caseation. The choroid is irregularly thickened over a large area, so that a lenticular mass is formed. The process continues to spread, usually from behind forwards. The lamina vitrea offers considerable resistance, and the process may come to a standstill. The granulation tissue then organises into a dense scar, from which the giant cells finally disappear.

More commonly the membrane of Bruch gives way, the retina is attacked, and may show typical giant-cell systems. The granulation tissue then proliferates into the vitreous, and the appearances much resemble glioma, especially glioma endophytum. In this manner the greater part of the globe may be filled with tuberculous material. Meanwhile erosion of the sclerotic occurs, the lamellæ being forced apart and destroyed. The tissue also follows the perforating vessels and nerves. More rarely it spreads into the optic nerve. Eventually the globe is perforated, usually in the anterior part, either at the corneo-scleral margin or under the conjunctiva, at the site of the perforating anterior ciliary vessels; less frequently perforation occurs posteriorly, near the vortex veins or at the entrance of the optic nerve (Fig. 340).



FIG. 340.—TUBERCLE OF THE CHOROID. $\times 3$.

From a girl, æt. 1. Extensive tubercle of the choroid, which has burst through the sclerotic. The retina and large areas of the choroid are necrotic. The mass consists of granular tissue with giant cells but few epithelioid cells; there are no typical tubercle systems.

Solitary or conglomerate tubercle is rare; it may in the early stages simulate sarcoma of the choroid, the retina being detached in the same manner. Optic neuritis may occur (Haab). The diagnosis, too, from glioma retinae may be extremely difficult or impossible (Brailey, Jung, Kunz, Emanuel, A. Knapp). These tubercular pseudo-tumours were well described by Mackenzie. The earliest microscopical examination is reported by v. Graefe of a pig's eye. The histological characters are the same as in the other forms, the mass being made up of more or less well defined giant cell systems lying in exuberant granulation tissue. The subsequent course is similar to that of the diffuse chronic form, usually going on to perforation of the globe. Resolution may occur in an early stage, with the development of a

white scar, generally surrounded by a densely pigmented zone, or the necrotic changes may be excessive, leading to shrinking of the globe. Perforation, however, is the usual result, which may be followed by infection and panophthalmitis.

MANZ.—A. f. O., iv, 2, 1858; ix, 3, 1863. BUSCH.—Virchow's Archiv, xxxvi. COHN-HEIM.—Virchow's Archiv, xxxix. v. GRAEFE AND LEBER.—A. f. O., xiv, 1, 1868. PERLS.—A. f. O., xix, 1, 1873. DINKLER.—A. f. O., xxxv, 4, 1889. BOCK.—Virchow's Archiv, xci. VERNON.—R. L. O. H. Rep., vi, 1868. B. FRÄNKEL.—Jahrbuch für Kinderheilkunde, ii, 1870; Berliner klin. Wochenschrift, 1872. LITTEN.—Volkmann's klin. Vorträge, cxix. WEDL AND BOCK.—Path. Anat. des Auges, Wien, 1886. MARGULIES.—Ein Beitrag zur Kenntniss der Miliartuberculose der Chorioidea, Königsberg, 1898. MACKENZIE.—Diseases of the Eye, London, 1854. v. GRAEFE.—A. f. O., ii, 1855. NEESE.—A. f. A., xvi, 1886. COUPLAND.—Trans. Path. Soc., xxv, 1873; Lancet, 1879. WEISS.—B. d. o. G., 1877; A. f. O., xxiii, 4, 1877. HAAB.—A. f. O., xxv, 4, 1879; Helmholtz'sche Festschrift, 1891. BURNETT.—A. of O., xii, 1883. S. MACKENZIE, BRAILEY.—T. O. S., iii, 1883. MULES.—T. O. S., iv, 1884. LAWFOED.—T. O. S., vi, 1886. SCHÖBL.—C. f. A., xii, 1888. WAGENMANN.—A. f. O., xxxiv, 4, 1888; B. d. o. G., 1891. LIEBRECHT.—A. f. O., xxxvi, 4, 1890; Münch. med. Woch., 1897. MANZ.—K. M. f. A., xix, 1881. PRÖBSTING.—K. M. f. A., xxix, 1891. JUNG.—A. f. O., xxxvii, 4, 1891. BACH.—A. f. A., xxviii, 1894. PANAS AND ROCHON-DUVIGNEAUD.—Recherches anat. et clin. sur le Glaucome et les Néoplasmes intra-oculaires, Paris, 1898. TATHAM THOMPSON.—T. O. S., xviii, 1898. TUYL.—K. M. f. A., xxxviii, 1900. KUNZ.—K. M. f. A., xxxix, 1901. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. EMANUEL.—K. M. f. A., xl, 1902. LÜTTGE.—A. f. O., lv, 1, 1902. *ZUR NEDDEN.—K. M. f. A., xli, 1903. A. KNAPP.—A. of O., xxxii, 1903. DUPUY-DUTEMPS.—A. d'O., xxiv, 1904.

LEPROSY

The choroid is affected secondarily to the ciliary body in leprosy. The bacilli are chiefly in the spaces between the fibres, and are especially numerous in the suprachoroidal space. The reaction of the tissues is slight; there are few wandering cells, and masses of granulation-tissue, such as occur in the iris and ciliary body, have never been observed. The bacilli often lie in the pigment cells, and along the nerves, especially in the maculo-anæsthetic cases. Clumps are also found near the vessels, particularly in the choriocapillaris: here there is frequently hyperæmia, with cedema and infiltration.

JEANSELME AND MORAX.—Ann. d'Oc., cxx, 1898. *BORTHEN AND LIE.—Die Lepra des Auges, Leipzig, 1899.

NODULAR CHOROIDITIS

Reference has already been made to the aggregations of lymphocytes, similar to those found in nodular iritis and cyclitis, which are present in most forms of chronic choroiditis, especially the sympathetic type.

Passauer and Leber have reported a case which they considered due to extension of trachoma. The anterior part of the eye was involved in a granulomatous proliferation, and the sclerotic was perforated. In view of the fact that no further evidence of similar extension of trachoma to the interior of the eye has been forthcoming, it is probable that the case was one of syphilis or tuberculosis.

PASSAUER, LEBER.—A. f. O., xix, 2, 1873.

DEGENERATIONS

SENILE CHANGES

The senile changes in the uveal tract have been exhaustively investigated by Kerschbaumer. Those occurring in the pigment epithelium of the retina may be conveniently referred to here. The pigment cells show changes which are partly regressive, partly hyperplastic. They occur earlier, and are most marked in the anterior portion, and were found in three quarters of all eyes examined over the age of 50. The cells become swollen and elongated, losing their hexagonal shape; the pigment becomes irregular, some cells being almost devoid of it, whilst in others it is heaped up, and the granules themselves lose their characteristic rod shape and become spherical. The cytoplasm becomes vacuolated, and contains droplets of fat; the nuclei stain feebly and disappear. Finally, the cell breaks up and the pigment granules are set free. Hyperplastic changes are shown by the proliferation of some of the cells. Many contain two nuclei, and groups of new, ill-formed cells appear. Associated with this proliferation is the formation of "colloid bodies" (*v. infra*), and thickening of the elastic lamina.

The changes which occur in the choroid proper are more marked in the posterior portion; indeed, it is probable that interference with the blood supply is responsible for the pigmentary changes being most marked anteriorly in the worst nourished part. In the choriocapillaris the capillaries become varicose, but on the whole narrowed, and their walls become thickened, so that the contours are better defined. These changes, accompanied by some hyaline degeneration, occur in patches, and may go on even to complete obliteration. Degeneration is also marked in the larger vessels, especially the arteries. The endothelium of the intima contains fatty globules, and the media and adventitia become thickened and striated. The muscular coat undergoes degeneration, partly of a fatty nature, and is replaced by fibrous tissue. The whole vessel wall may become hyaline, the lumen being much restricted or even obliterated. The elastic tissue persists longest and increases in amount, as is well shown by specific elastic tissue stains.

Kerschbaumer also noticed increase of leucocytes in the perivascular lymphatics, especially of the vortex veins, such as have been described in glaucoma.

SATTLER.—A. f. O., xxii, 2, 1876. KUHNT.—B. d. o. G., 1885. *KERSCHBAUMER.—A. f. O., xxxviii, 1, 1892.

ATROPHY

It has already been pointed out that subacute and chronic choroiditis and even the less virulent types of acute choroiditis, find their natural termination in the formation of scar tissue: that further, the cicatricial tissue involves the destruction of the normal choriocapillaris and many

of the original vessels, and that the new-formed vessels finally undergo degenerative changes, whereby they become converted into fibrous strands; and again, that the fibrous tissue which thus replaces the choroid itself degenerates, contracting into thin bands or laminæ, or forming hyaline whorls or small clumps. The exudates may also become hyaline, and appear as round or irregular masses of varying size. Finally, ossification may occur (*v. infra*).

These changes may be localised (Fig. 341), as in choroiditis disseminata, or they may involve the whole choroid. In this manner the choroid may be replaced by a thin, dense fibrous tissue membrane, with sparse elongated nuclei, and possessing few or no blood-vessels. A very high degree of atrophy follows prolonged increase of intra-ocular tension.

Atrophy, equally intense, but of a different type, is found in shrunken

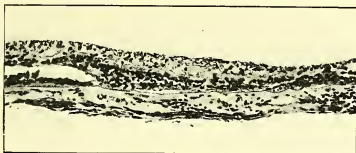


FIG. 341.—RETINO-CHOROIDAL ATROPHY. $\times 120$.

From a man, æt. 42, with ciliary staphyloma following iridectomy twenty-five years before. Patch of retino-choroiditis; adhesion and atrophy of the two membranes.

globes. Here the degenerated choroid is pulled inwards and folded over or raised into papilliform projections by the contraction of organising cyclitic exudates. Owing to the highly albuminous exudates in the choroid itself excessive quantities of new fibrous tissue are often formed. These solidify and undergo regressive—hyaline and other—changes, forming dense masses in some parts, whilst in others they are dragged out into loose networks, which in the earlier stages are richly supplied with blood-vessels. Ultimately ossification ensues.

VASCULAR DEGENERATION

Apart from the vascular degeneration which occurs as the result of inflammatory processes (q. v.) or old age (q. v.), special forms are seen, usually associated with general disease of the vascular system. The arteries are most affected, showing hyaline degeneration of their walls (in nephritis, etc.), perithelial proliferation, miliary aneurisms, hyaline thrombi, etc.—in nephritis, lead-poisoning, etc. (Duke Carl Theodore, Oeller). Arteriosclerosis and endarteritis obliterans are found, *e. g.* in granular contracted kidney, lead-poisoning, etc., showing the characteristic changes (*see* "Optic Nerve") (Fig. 342). Endarteritis obliterans may result from localised interference with the blood flow,

and may therefore be partial in distribution (Ischreyt). It may also be caused by septic processes (Ginsberg).

The veins show less change, though perivascular infiltration is often more marked; elastic and hyaline degeneration of the walls also occurs. The capillaries show thicker hyaline walls, with sharp, but irregular contour, best seen in flat preparations. They are sometimes filled with hyaline thrombi, and then present a bizarre appearance. They may



FIG. 342.—VASCULAR DEGENERATION IN THE CHOROID. $\times 55$.

From a man, æt. 56; eye excised for hypopyon ulcer. The endothelium of the intima is much thickened, the lumen of the vessel being occluded in many cases.

be obliterated in patches, so that capillaries with patent lumina pass directly into fibrous strands.

OELLER.—Virchow's Archiv, lxxxvi, 1881. HERZOG CARL THEODOR.—Ein Beitrag z. path. Anat. des Auges bei Nierenleiden, Wiesbaden, 1887. ISCHREYT.—A. f. A., xxxvii, 1894. GINSBERG.—Grundriss d. path. Histologie des Auges, Berlin, 1903.

“COLLOID BODIES”

In the eyes of elderly persons—occasionally after 30, frequently after 40, and almost constantly after 60—and in cases of chronic choroiditis, especially in phthisis bulbi, globular thickenings are seen upon the inner surface of the membrane of Bruch, covered by irregular, more or less degenerated pigment epithelial cells (Fig. 344). These have been called “colloid bodies” (Drusen). The white spots in the so-called retinitis punctata albescens (Mooren) are probably due to “colloid bodies.”

These hyaline bodies early attracted attention, having been noticed by Wedl and Virchow; they were first carefully studied by Donders (1855) and H. Müller (1855). Donders regarded them as colloid degeneration of the nuclei of the pigment epithelium; Müller considered the changes in the epithelium secondary to the thickening of the lamina vitrea. de Vincentiis (1874) was of the opinion that whichever view was adopted the degeneration was one of the cell as a whole rather than of the nuclei. Modern opinion, with the exception of de Schweinitz, has been in favour of primary degeneration of the cells, and not of an inert membrane such as the lamina vitrea.

Leber first accurately described the structure of the bodies, and later gave it as his opinion that the hyaline material was of the nature of a cuticular substance produced by the pigment-cells. Meyer thought

that the elevations caused by the fusion of the hyaline droplets stimulated the cells by displacing them, and led to increased secretion. Alt (1880) held that the Drusen were not only a product of secretion, but that the cells themselves became transformed into hyaline bodies. da Gama Pinto (1892) thought that the cells first proliferated, forming groups, in the centre of which the products of secretion collected. Birnbacher and Czermak (1884) found that the bodies stained like hyaline material elsewhere with picrocarmin and eosin. Kerschbaumer (1892) drew attention to the granules in the thickened vitreous membrane in old people. These appear as strongly refracting points, reaching the size of a nucleus. They become grouped together, and thus form the basis of a hyaline body; these in turn become fused together, forming nodules of considerable size. The author, from the



FIG. 343.—PHTHISIS BULBI. $\times 4\frac{1}{2}$.

From a youth, æt. 17. Lens calcareous; retina detached; choroid studded with "colloid bodies."

reactions of the granules and Drusen to eosin, picrocarmin, and fuchsin, considered that they were a hyaline material manufactured by the pigment-cells. Greeff (1903) considers that the changes in the cells are primary, and that they are caused by interference with nutrition, due to changes in the choriocapillaris occurring, not only in old age, but also in pathological conditions. Schieck (1904), from a study of the earliest stages of Drusen formation, concludes that they are neither cuticular products of the pigment-cells nor thickenings of the lamina vitrea, but are due to degeneration of desquamated cells. Contrary to most observers, he does not think that the bodies are covered with epithelium at first, but that this proliferates over them at a later stage. Fresh cells may accumulate on the surface and undergo the same change, thus causing concentric layers, separated by streaks of pigment.

In the centre of the hyaline body there are often faint rings representing, according to Schieck, the original nuclei. Rumschewitsch (1904), with whom the majority of pathologists will probably agree, accepts the theory of a cuticular secretion from the pigment-cells, admitting, however, that in the later stages the greater part of the cytoplasm of the cells may degenerate and form hyaline material; the nuclei and the perinuclear protoplasm persists and contributes to the formation of the pigmentary capsule.

The superficial capsule of pigment has also been explained in various manners. According to H. Müller the pigment cells atrophy, and only free pigment remains. Leber says that the whole surface is covered with cells containing a black pigment, the molecules of which are larger than normal, round or irregular and not rod-shaped, and confined to parts only of the cells, not equally distributed throughout them. The earliest nodules have a pigmented epithelial covering. Meyer agrees that there is a complete capsule, whilst the majority of authors, including Alt, Fuchs, Pagenstecher, and Ginsberg consider

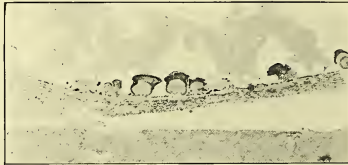


FIG. 344.—“COLLOID BODIES.” $\times 34$.

From the same specimen. Note the covering of pigment epithelium.

that the cells may be absent in places. It is difficult to be certain of this point, for the distribution of pigment is very irregular and affords insufficient evidence as to the extent of the protoplasm. The pigment is at first aggregated around the nuclei (Rumschewitsch), and this probably accounts for Schieck's description; soon densely clumped pigment pervades the cells, as first described by Leber. He also noted the heaping up of the pigment at the periphery of the bases of the Drusen, so that it appears there to have several layers. Later the pigment becomes rarefied in places over the nodules, and may finally disappear. The presence of a complete epithelial capsule is best demonstrated by triple staining with borax carmin, picric acid, and indigo carmin (Rumschewitsch).

The nodules have first a finely granular structure, as Kerschbaumer pointed out; later they become homogeneous. Neighbouring Drusen frequently fuse together, so as to form long masses with a wavy surface, covered with epithelium; this condition is most found near the ora serrata. Large isolated hyaline bodies are usually round or oval, often attached to the choroid by only a narrow stalk. They do not long remain homogeneous, but faint nucleus-like outlines are seen, and

especially a definite concentric lamination (Alt, Pagenstecher); the layers are often elliptical and excentric. In still later stages infiltration with calcareous matter occurs, first observed by H. Müller; it may be seen only in the centre or irregularly, as fat-like globules, or the whole nodule may be calcified. Finally, the bodies may become ossified; this is brought about after destruction of the underlying membrane of Bruch by the invasion of connective tissue from the choroid (Fig. 348). This tissue, as is well known, contains cells which are capable of becoming osteoblasts; it insinuates itself between the pigment epithelium and the main mass, forming regularly disposed layers. The intercellular substance increases and shows an extremely fine fibrillation, staining deeply with carmin and deeply but diffusely with hæmatoxylin. True bone is ultimately developed in exactly the same manner as in the choroid (*v. infra*).

The condition of the lamina vitrea under the hyaline bodies is of



FIG. 345.—A "COLLOID BODY." $\times 200$.

Coats, R. L. O. H. Rep., xvi. Stained with hæmatoxylin and eosin. It appears as a simple sessile bulging of the membrane of Bruch. It is covered by a single layer of flattened pigment epithelium.

some interest. According to H. Müller it is thickened, but this is common to old age, and Meyer pointed out that the bodies were not confined to the thickest parts. Most illustrations show a distinct line between the bodies and the lamina (Alt, Greeff, Ginsberg, Coats), and da Gama Pinto considered that the bodies were really independent of the membrane. It is probable that the membrane of Bruch is a cuticular membrane formed from secretion of the pigment epithelial cells; in pathological conditions the cells are subjected to chronic inflammation, whereby they are stimulated to produce an abnormal amount of secretion.

As regards the conditions in which hyaline bodies are found on the surface of the choroid, old age takes the first place (H. Müller, Kerschbaumer). They have, however, been seen in youth (12 years, Alt). They have also been found in syphilis (Fuchs), in chronic glaucoma (Birnbacher and Czermak), in pseudoglioma (Schieck), in incomplete atrophy of the globe (Pagenstecher, Rumschewitsch), in cases with degeneration of the retinal pigment (Leber), after trauma (da Gama Pinto), and commonly in shrunken globes. They have been

found at an early stage in retinitis pigmentosa (see "Hyaline Bodies at the Optic Disc"). Rarely they have been seen associated with acute suppurative choroiditis (Schweigger, Knapp). In the more pathological types they may be most numerous in the affected regions, but they are more commonly distributed as in old age, *i. e.* with a preference for the neighbourhood of the ora serrata and around the optic disc.

In size they may reach a diameter of 1 mm., but are rarely more than 0.5 mm. The attachment to the choroid may be very fine, and they not infrequently get free, so as to be isolated in the retina or even vitreous (Meyer): they are sometimes found on the outer surface of a detached retina.

Coats has recently investigated the origin of colloid bodies of the choroid. His conclusions, with which I fully agree, are deduced from a philosophical review of the facts, which merits repetition here.

Certain theories may be put aside as discredited or inherently improbable, such as Rudnew's, that the bodies arise from hyaline degeneration of wandering leucocytes, and Pes's, that they may arise by processes of sclerosis and atrophy in superficial papillæ of the choroid formed in consequence of the cicatricial contraction following upon inflammation in the middle and deep layers of the tunic. The theory of Hofmann may be merely mentioned; this author states that they arise from hyaline degeneration of thrombi in the choriocapillaris vessels, or of the endothelial cells lining their walls. The hyaline masses so formed project in their growth against the membrane of Bruch and finally rupture it, and



FIG. 346.—A "COLLOID BODY," $\times 200$. Coats, R. L. O. H. Rep., xvi. Stained with Weigert's elastic tissue stain. A strongly marked line runs past it—the outer layer of the membrane of Bruch. (Cf. Fig. 323).

pass through to the inner side, after which, so says Hofmann, the membrane heals up and an appearance is produced as if the membrane of Bruch ran past the excrescence unchanged. This appearance undoubtedly occurs (Fig. 346), and has been the cause of much of the controversy, since it has led many to deny to the bodies any connection histologically or developmentally with the membrane of Bruch.

No one who has examined many of these excrescences will be inclined to consider these three theories when he notes how strictly confined the bodies are to the inner layers, and how they not infrequently occur in choroids quite free from all traces of inflammation, past or present. Leaving these explanations, therefore, out of consideration, opinions will be found to be divided into two main camps: (1) The excrescences arise from actual transformation of the cells of the pigment epithelium. (2) They arise, as the membrane itself is supposed to arise, as a deposit from the cells of the pigment epithelium, but without actual transformation of pigment cell into excrescence. The former of these may be conveniently referred to as the "transformation" theory, the latter as the "deposition" theory. The trans-

formation theory, which was first enunciated by Donders, has, perhaps, the most supporters, and seems to be most favoured by recent investigators, at least in Germany.

The details of the process are variously given by different authors. Donders believed that the nucleus became hyaline, and so formed a minute excrescence, but it was afterwards pointed out by de Vincentiis that it was more consonant with general pathological principles that the protoplasm should be first attacked by a degenerative process. Since the colloid bodies were found mostly in the eyes of old people, it was natural to connect them in origin with the well-known senile changes in the epithelium. It was therefore explained that the pigment epithelium became irregular in its arrangement, some of the



FIG. 347.—“COLLOID BODIES.” $\times 200$.

Coats, R. L. O. H. Rep., xvi. Two large laminated “colloid bodies,” stained with hæmatoxylin and eosin. Beneath them, and apparently quite unconnected with them, is a fine, highly refracting zig-zag line—the outer, elastic layer of the membrane of Bruch. Note the unbroken layer of flattened, partially depigmented epithelium covering the nodules.

cells being larger than others and sometimes containing two nuclei; the layer might also be doubled. In addition the pigment was irregularly distributed, denser in some places and thinner in others, while the little rods normally found were replaced by round granules. Certain of these pale cells became more and more homogeneous, lost their nuclear staining, and finally became converted into small colloid bodies which grew by accretion. Or, according to others (*e. g.* Dimmer), colloid globules appeared within the cell-protoplasm which, becoming larger by confluence, finally destroyed the cell and formed a minute colloid body, the larger being the result of the fusion of many smaller.

There are many difficulties in accepting this theory of origin. In the first place the histological appearances do not support it, for in an

early stage the bodies, if stained in the usual manner with eosin, have the appearance of being thickenings of the membrane itself, provided that the section passes through their middle (Fig. 345). They seem, however, early to form a knob-like head, and if this is cut peripherally, the nodule will naturally seem to have no connection with the membrane of Bruch. Again, while it is true that the pigment epithelium in many cases shows alterations, these have no constant relation in distribution to the colloid bodies, as has been shown by Kerschbaumer, and are to be regarded, like the colloid bodies themselves, as pathological, or in some cases as senile changes. The proof of cause and effect, therefore, is inadequate, and definite transitional forms have not been sufficiently clearly described and figured. Another very serious difficulty consists in the fact that the bodies, even when of large size,



FIG. 348.—OSSIFYING "COLLOID BODIES," $\times 55$.

From a specimen by Snowball. Note the preliminary invasion of the base by fibrous tissue.

remain covered with epithelium, often flattened and depigmented, but seldom broken through (Fig. 347). Why should this be so if they arise from one or several pigment cells? Would the swelling cell not rather push its neighbours aside and remain uncovered? The explanation has been put forward that adjacent cells grow over, but why should they do so, and if they do, why should they form in so many instances a single uniform layer? It is surely more likely that the excrescences have a uniform covering because they originated underneath the epithelium and merely raised it up. Over small nodules the epithelium will often be found to all appearance quite unaltered. Another explanation, still more unlikely, is that only part of the cell becomes involved in the degeneration, while the nucleus and unaffected part of the protoplasm form the well-stained lining. But this is surely supposing

an event very unlikely in the life-history of an individual cell, nor are the cells firmly adherent to the excrescences as they ought to be if the latter were formed from part of their protoplasm.

Again, the size to which single nodules may grow (Fig. 347) is against their origin from one cell and strongly in favour of an origin by deposition or secretion; no case of a cell expanding to so great a size can be produced in pathology. The remark does not, of course, apply to tuberculated or compound nodules such as are often found, since these might arise from the fusion of many cells. Nor does this exhaust the indictment against direct transformation; in the earliest stages the excrescences never separate with the pigment epithelium, but always remain firmly attached to the membrane of Bruch, although it is said that when large and standing upon a thin pedicle, they may break off and even be found in the outer layers of the retina. Again, Donders himself has shown that they react in all respects to reagents like the membrane itself, being highly resistant to water, alcohol, ether, acids, alkalies, mechanical injuries, etc., and failing, like the membrane itself, to take on the stain for amyloid substance.

A chain of arguments is thus raised against an origin by direct transformation, each link of which seems to furnish proof for the second theory, that the excrescences are formed by deposit from the cells of the pigment epithelium in the same manner as in all probability the membrane itself is formed. The case in favour of this hypothesis, which was first stated by Heinrich Müller, may be stated thus: In an early stage the bodies appear histologically to be simple localised bulgings inward of the membrane; they show no constant relation in localisation to those changes in the pigment epithelium, found in old and diseased eyes, which have been described as intermediate in the process of transformation; single nodules may grow to a large size while still remaining covered with a well-marked unicellular layer of epithelium; they do not separate with the epithelium when the latter strips off; they react to chemical, mechanical, and staining agents in all respects like the true membrane. In addition the analogy of the outgrowths of the membrane of Descemet may be cited. These also show no appearance of arising by transformation of the endothelial cells, but present themselves as localised inward bulgings of the membrane itself, lined by a well-preserved single layer of endothelium. In the case of the membrane of Descemet also, the proof is very complete that the endothelial cells are capable of laying down homogeneous substance, witness the membranes which sometimes form on the front of the iris in cases of anterior synechiæ (*see* Vol. I, p. 304). The case of the lens capsule furnishes, perhaps, an even more complete analogy, since, like the membrane of Bruch, it is lined by epithelial cells of epiblastic origin, and it has been shown that these cells also are capable of laying down new homogeneous substance (*see* "Anterior Capsular Cataract").

How, then, are we to explain the statement, so often and so definitely made by supporters of the transformation theory, that the membrane of Bruch can be seen to run past colloid bodies and to take no part in their formation? If it can really be shown to be so, then in spite of the arguments adduced above to show that they *ought* to arise from that

membrane, we must either admit checkmate or find some new mode of origin for them. Nor can the statement be dismissed as founded upon a mere error of observation. There is such an appearance, as may be very clearly seen in Figs. 346 and 347. Allusion has already been made to the fact that this would be produced if the nodule had a slender pedicle and a large expanded head, and if the periphery of this head were cut by the section, but not the pedicle. This, no doubt, is the explanation in some cases, but not in all, for it is a matter of experience that small excrescences, at least, are sessile, yet even in these the membrane of Bruch seems to go past unaltered (Fig. 346). There is, however, another and most important factor in the structure of the membrane itself, a factor which seems to furnish the solution of the problem. In sections of ordinary thickness, prepared and stained in the usual manner, this membrane appears homogeneous or slightly granular (Fig. 322). Yet even in early descriptions (Sattler, etc.), a finely reticular appearance of the outer aspect and a tendency to split into two layers on macerating with strong salt-solution were noted. The key to this appearance has been given by methods of special staining. The reticular appearance is, in fact, due to a layer of very fine elastic fibres. In specimens stained with Weigert's elastic tissue stain, this is very plainly brought out (Fig. 323). The separation into two layers is most distinct in the neighbourhood of the papilla where the membrane of Bruch is thickest, and the distinction is further emphasised here by the fact that the two portions end differently. The inner homogeneous portion next the pigment epithelium ends with the ending of the pigment epithelium, a further proof that it is a product of these cells. The outer elastic portion, which can easily be seen with high magnification to be composed of a feltwork of exceedingly fine sharply stained elastic fibres, goes on into the substance of the papilla for some little distance, and finally terminates with a curious curly upturned end (Fig. 323). It may be remarked in passing that Weigert's elastic tissue stain is specific only for elastic fibres and the *elastica interna* of vessels. A certain diffuse blue staining of a membrane, usually regarded as "elastic," is no proof that it contains the same substance as the true elastic fibres and membrane of Henle. For instance, the membrane of Descemet, the zonula, the lens capsule, the dilatator iridis, the sphincter pupillæ, and the homogeneous portion of the membrane of Bruch, all stain diffusely, but do not take on the intense blue staining which is characteristic of true elastic tissue.

A further proof of the composite nature of the membrane of Bruch is furnished by its method of terminating towards the ciliary body (*see* Vol. I, p. 334).

The above details have been given in order to show that the membrane of Bruch, which seems homogeneous when stained with eosin (Fig. 322), can be resolved into two layers by special staining (Fig. 323). It seems highly probable that the difference represents a difference in origin. The fine elastic fibres of the outer layer are in all respects similar to the elastic fibres found in the neighbouring choroid, and must, therefore, be looked upon as contributed by the choroid, since it is difficult to believe that definite elastic *fibres* could be laid down by

the epiblastic pigment epithelium. The inner homogeneous layer, on the other hand, has all the appearance of a cuticular product laid down by the epithelium in the same manner as the lens capsule is laid down by its epithelium. The probability is therefore strong that it has been contributed by the pigment epithelium. It may be said that only the inner homogeneous layer ought to be reckoned as the membrane of Bruch (or lamina *vitrea*), and no doubt this would be convenient, but the present point is that the "membrane of Bruch" as seen in sections stained in the usual way includes both layers.

Applying now these observations to the elucidation of the origin of colloid bodies, it will be found that there is much evidence in favour of the view that they arise from the inner homogeneous layer and from it alone. The argument would run somewhat as follows: The homogeneous portion of the membrane of Bruch is a cuticular product from the pigment epithelium, and in a similar manner, under the influence of certain pathological stimuli, these cells may lay down irregular nodules of the same substance. On the other hand, the elastic portion is a mesoblastic product belonging in reality to the connective tissue of the choroid, and takes, therefore, no part in the formation of this secretion, but passes the nodules unthickened and unaltered. Since, however, it is homogeneously stained with eosin, an appearance is presented as if the membrane of Bruch went past unchanged and without having any connection with the colloid mass (Fig. 346). Hence has arisen the view that these excrescences are in origin wholly independent of the membrane of Bruch. Staining with Weigert's elastic tissue stain, however, will be found to solve the problem for the unaltered membrane, which will be found to be only the outer elastic layer of the membrane of Bruch, while the colloid body is a true bulging of the inner homogeneous portion, and, like it, does not stain specifically with Weigert.

The formation of colloid bodies, however, is not the only instance of a pathological process which affects the two layers in a different manner. In general the elastic layer is more resistant than the other to noxious influences, and in some cases of chorio-retinitis it will be found that in the situation of an inflammatory patch the homogeneous portion is eroded while the elastic layer persists, or that when both have ruptured the elastic layer can be traced for a considerably longer distance than the other. An excellent instance of the different reaction of the two layers to pathological influences will be found in a case of sarcoma of the choroid reported by Nettleship (*v. infra*, "Sarcoma"). A figure (Fig. 370) is given, showing very clearly the homogeneous or faintly laminated inner layer and the wavy strongly marked outer layer. There can be no doubt that the "epithelium-bearing membrane" is nothing else than the homogeneous portion of the membrane of Bruch—indeed, a large number of colloid bodies spring from it. The "very undulating highly refracting line," on the other hand, is the outer elastic layer. The case, therefore, furnishes the strongest possible proof of the composite nature of the membrane of Bruch and of the origin of colloid excrescences from the inner layer of it.

The conclusion is, therefore, in favour of the deposition theory as

opposed to the transformation. Both theories have, however, this in common, that they presuppose an abnormal metabolism in the pigment epithelium. What the stimulus or lack of stimulus may be, which results in this altered metabolism one cannot presume to say. It is in part, no doubt, definitely pathological, since colloid bodies occur very constantly in eyes the subject of extensive destructive changes, but in part also it is to be regarded as almost a normal change, since they occur in a large proportion of senile eyes. Without wishing to draw any close analogy, a comparison may be instituted between these changes and the changes which occur in endarteritis. In the latter case also the lesion may be a definite response to a pathological stimulus (in the neighbourhood of gummata for instance), or may, on the other hand, be almost regarded as a normal senile change.

Cases which have been both seen clinically and examined pathologically are rare in the literature. Liebreich described the first in 1858, and the only other which I have been able to find is one by Nagel in 1875—the year in which Hutchinson and Tay described the condition since known in England as “Tay’s choroiditis.” They correctly conjectured that this was due to these excrescences. Coats has been able to observe them clinically in one eye, and to find them microscopically in the other eye of the same patient, and possibly this is not an uncommon experience.

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OSSIFICATION

Ossification of various parts of the eye was very early described; it was the subject of a paper by Schön in 1838, and was investigated by Arlt in 1847. The latter considered that ossification of the choroid was really calcification of exudate between the choroid and retina. Hulke (1857) first proved the occurrence of bone in the eye, and Förster first figured typical bone in the choroid with definite Haversian systems.

The earliest important paper on the subject was by Pagenstecher (1860). He proved that the bone originates in new-formed fibrous tissue or in the normal tissues after they have undergone atrophic changes, and that it grows in the same manner as the normal periosteal bone. Knapp (1871) first investigated the question of the exact site of origin, and arrived at the conclusion that it was the choriocapillaris. He pointed out that bone formation usually ceases at the ora serrata,

i. e. where the choriocapillaris stops. He further stated that other parts of the uveal tract and of the eye—sclerotic, retina, vitreous, lens—do not undergo ossification. Whilst substantially correct in his deductions, Knapp did not sufficiently explain the apparent formation of bone in other parts of the eye, nor was he accurate in limiting its formation to the choriocapillaris. This was pointed out by Schiess-Gemuseus (1873), who showed that it usually arose in the masses of fibrous tissue which replaced the atrophied choroid.

Ossification is the final stage of degeneration of the organised inflammatory deposits of plastic choroiditis. It may therefore be found in any of the conditions which give rise to widespread chronic choroiditis, but is especially frequent in cases in which cyclitis has been the prominent early feature. It is hence most often observed in shrunken globes. It occurs at all ages, from childhood (11 years) up to extreme old age (102 years). The time required for the growth of the bone is, in most cases at least, several years, but Schiess-Gemuseus records a case in which bone was found in the choroid of an eye that



FIG. 349.—BONE IN THE CHOROID.

After Lawson. In A the bone almost fills the globe. In B the deposit is chiefly near the disc.

had been normally functional only ten months before, and Leslie Buchanan in the eye of a boy ten weeks after injury.

The bone in the slighter cases is irregularly distributed, but has a tendency to start at the edge of the disc (Figs. 349, B, 350), and is usually thicker here in more advanced cases. It is most frequently limited anteriorly by the ora serrata; in old cases the whole choroid may be ossified and changed into a shell of bone, thicker at the posterior end, where there is a hole representing the position of the optic nerve (Fig. 349, A). The bone may form bars of compact substance, which may be united to one another by smaller bridges, the interstices being filled with granulation tissue, or larger compact masses may be formed with the typical structure of an ordinary long bone, with well-developed Haversian systems, the lamellæ with their bone-corpuscles being arranged concentrically around the blood-vessels. Finally, a true medulla may be formed, composed of vascular adipose tissue (Fig. 356), but this is not very common.

As a result of the chronic plastic inflammation in the choroid, the outer pigmented layers are reduced to a fibrous band containing fewer large vessels, which exhibit more or less marked fibrous thickening of their walls; the inner layers, *viz.* the choriocapillaris and membrane

of Bruch, on the other hand, are for the greater part absent in those areas where bone develops in the layer of fibrous tissue which has become organised from exudation thrown out towards the inner surface of the choroid. In these areas the capillary layer, where it is still present, is never a continuous one, but at most is represented by only a few vessels that lie along with other new-formed capillaries in a layer of fine fibrous tissue, where fibrous tissue remains between the plate of bone formed in it and the outer atrophic pigmented stroma. The membrane of Bruch, however, has disappeared altogether in these parts, and here the exudation had been greatest and the inflammatory process presumably most intense. In none of the cases is this homogeneous membrane found lying on the choroidal side of the bone-con-



FIG. 350.—BONE AT THE OPTIC DISC. $\times 50$.

Calcareous and bony deposits in the choroid close to the edge of the disc; they push forwards the retina. This is a very early stage of ossification of the choroid.

taining fibrous layer. Where it is still present near the bone, viz. close to the end of the expanding plate, or contiguous to the focus of early ossification, the membrane of Bruch lies *internal* to the bone, the latter taking the place of the choriocapillaris (or the layer of small vessels, Sattler's layer as well), and either lying immediately between the vitreous lamina and the choroidal stroma or separated from them by a layer of fibrous tissue. The bone, therefore, develops in fibrous tissue that replaces the choriocapillaris, or where it is still present, in the fibrous tissue that has been heaped up on its inner side and has destroyed the lamina vitrea. Where the fibrous tissue forms a thick mass uniting the choroid and retina, the bone may then appear to be quite internal to the choroid. The inner surface of the bone is usually lined by a layer of dense, richly nucleated, but poorly vascular con-

nective tissue, which in places shows the presence of choroidal pigment among its fibres. In the cases where the retina has become detached from the choroid the retinal pigment layer over the area of ossification is either absent altogether or represented by cells that are mostly degenerated and almost devoid of pigment. Where the fibrous layer unites the choroid and retina the pigment epithelium has proliferated more or less extensively, and lies internal to and separate from the ossified mass.

In the layer of fibrous tissue lining the external border of the bony plate one often sees a number of rounded bodies of various sizes. They are well defined, granular, and not striated in appearance, and lie either singly or united to each other or to the end of a trabecula of bone;



FIG. 351.—BONE IN THE CHOROID. $\times 60$.

From a specimen by Snowball, showing hyaline masses becoming calcified.

they do not take up any distinctive stain, as, *e. g.*, that for amyloid degeneration, but stain readily with hæmatoxylin; they look not unlike the colloid bodies seen on the surface of the choroid in other parts, and from that point of view might be taken for the remains of the membrane of Bruch which had elsewhere disappeared; in places clumps of pigment are seen in their neighbourhood, or pigment granules may be attached to them. As to their nature, they are probably masses of exudation that have undergone hyaline degeneration (*cf.* similar bodies often found in the cornea) and have evidently become in part calcified (Fig. 351). Fontan describes somewhat similar bodies, which he also considered to be exudates that had become calcified. He thought that from their number they had a part in the ossification of the adjacent fibrous layer as “stores of the calcareous elements for ossification”; he found them

only where the osseous layer was incomplete or showed no cancellous tissue. Such bodies may, however, be seen imbedded in the bone itself (Snowball).

In most cases the bone is formed in the posterior part of the choroid round the entrance of the optic nerve, but it may begin at some distance from the optic disc. Possibly the entrance of the short ciliary arteries into the globe here may have some connection with the increased exudation. Independent foci may be seen at other parts of the choroid or in the colloid bodies on its surface. In ossification of colloid bodies their substance is replaced by fibrous tissue, in which the formation of bone then takes place. This is comparable to the process of ossification in the lens. The formation of bone is not confined to the choroid: it often appears in the detached retina and in cyclitic membranes, it may surround the lens, and actually penetrate its capsule, or it may form a mass that occupies the whole of the vitreous chamber.

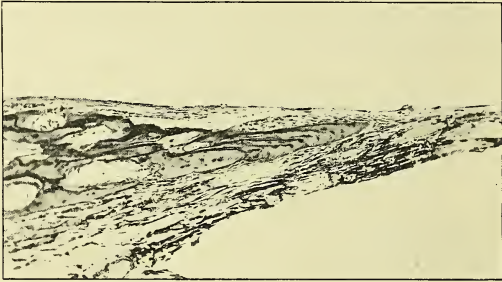


FIG. 352.—BONE IN THE CHOROID. $\times 55$.

From a specimen by Snowball, showing the relation to the membrane of Bruch, which runs over the inner (upper) surface.

Bone in the choroid is never developed through cartilage, but is always of the periosteal type. The first step in the conversion of the fibrous tissue into bone is seen in the more homogeneous, or finely granular, denser appearance that it assumes; it stains with eosin more brightly than the unchanged fibrous tissue. In this, the so-called osteoid stage, very few cells are seen in its substance, but already the cells at the border of the mass begin to assume an angular shape. When the deposit of lime salts takes place this osteoid tissue now appears roughly granular, and is deeply stained with hæmatoxylin; and as it merges into the more fully developed bone it again becomes clear and takes on the eosin stain, the spaces enclosed by the trabeculae being lined by a layer of cells, the osteoblasts. The end of a growing trabecula of bone is often seen to merge into a richly nucleated fibrous bundle. Where the fibrous tissue has attained some thickness towards the inner surface of the choroid, ossification appears to begin in its

outer layers first, so that they exhibit the lamellated structure and Haversian systems of fully developed bone, when its inner layers show only small trabeculæ that still have a fibrous appearance and possess only a few lacunæ and canaliculi with their corpuscles.

Different views have been put forward as to the origin of the osteoblasts. Stöhr, as quoted by Whiting, thought that "they are embryonic cells with a tendency to bone-formation which deposit themselves by preference at points involved in such metamorphosis." These are presumably conveyed to the eye from the periosteum of the orbit or some other region. This view had also been put forward by Busch, but is refuted by Kassowitz. Regarding the conversion of connective tissue into bone, Stöhr remarks: "Single connective-tissue fibres



FIG. 353.—BONE IN CYCLITIC MEMBRANE. $\times 55$.

From a specimen by Snowball. Ciliary body above, with cyclitic membrane pulling ciliary processes inwards; there is a nodule of bone near the anterior surface. Note the calcified "colloid body" below, surrounded by pigment epithelium.

become calcified, and on these are deposited osteoblasts, originating from embryonic cells, forming, after the manner described, bone." Grandclément suggested that the embryonic cells, that still remain in the choroid from foetal life, are stimulated into growth by the long-standing inflammation or irritation, and form fibrous tissue and then bone. Reid and, more recently, Buchanan have expressed the opinion that the connective-tissue corpuscles are converted into real bone-corpuscles. This appears to be the most likely view, for the cells of the fibrous tissue are frequently seen to take on an angular shape, and as they become more deeply imbedded in the young ossified tissue are evidently converted into true bone-corpuscles. Pagenstecher had long before suggested that the bone-corpuscles might arise, among

other sources of origin, from the cellular elements of the choroid. It is, however, not yet clear whether these connective-tissue cells are ultimately derived from the fixed cells of the choroid or from the cells of the capillary walls. Any connective tissue, it is said, may be converted into bone, yet it is difficult to say what are really the factors that determine the commencement of such a change in the fibrous tissue that forms in the choroid or other parts of the eye. In his study on 'Normal and Pathological Ossification,' Kassowitz found that while this process is always dependent on the development of blood-vessels in the ossifying tissue, it can only begin when this tissue has given up its expansive growth, and when simultaneously, or soon afterwards, the vascularisation of the tissue comes to a standstill or recedes. This

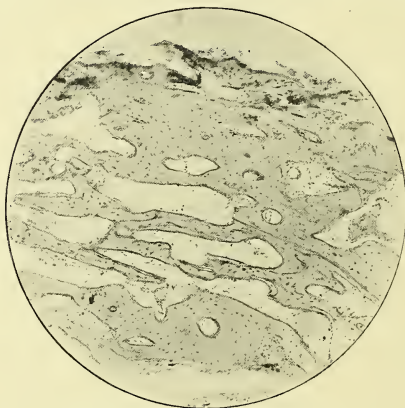


FIG. 354.—BONE IN THE CHOROID. $\times 55$.

From a specimen by Snowball. Part of a thick shell of bone in the choroid.

diminution in the blood-supply to the part concerned he believed to be common to all pathological ossification. Yet he admitted that his theory did not explain why ossification does not set in in every possible case. Dürr and Schlegtendal looked upon the presence of a plate of bone between the choroid and retina in a case of hydrophthalmos as a proof of the diminution of the blood-supply, and this diminution they attributed to the folding of the sclerotic by the external ocular muscles. In applying Kassowitz's description of ossification to the eye, Goldzieher expressed the opinion that the vitreous lamina and the substance lying between the vessels of the choriocapillaris are really finely fibrillar in structure, and thus act as a filter to the blood-plasma, weakening the current and thereby favouring the deposition of the lime salts. But, apart from this view of the structure of these parts, their action as a

filter cannot be taken as an essential factor in the production of bone in the choroid, because the lamina vitrea is so often entirely absent, and the bone not infrequently forms on its external surface, where it still remains.

Knapp, as already stated, came to the conclusion that the choriocapillaris is the place of origin of bone in the choroid. "In a low stage of development," he says, "the ossification begins in small plates, which lie in the choriocapillaris and are covered by the hyaline membrane and the pigment epithelium." He says further: "In a more advanced stage the more abundant exudation wrinkles and perforates the hyaline membrane, invests the inner surface of the choroid, and is

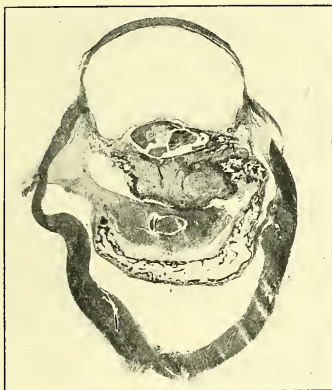


FIG. 355.—BONE IN THE CHOROID. $\times 3$.

From a man, æt. 28. Keratectasia and cyclitis following measles at age of 5. Note from before backwards, dome-shaped cornea as in buphthalmia, retracted iris, cataractous and calcareous lens, cyclitic membrane, detached retina, mass of fibrous tissue, and bony choroid with true medullary spaces. The space between the choroid and sclerotic is probably an artefact.

gradually converted into osteoid tissue." And in this view Knapp is supported by not a few writers (Pagenstecher (Case 2), Whiting, Reid, Lagrange). Berger says: "In the cases which we have observed at the beginning of the ossification, we have found that the vitreous lamina covering the internal surface of the choroid was preserved. The choriocapillaris was no longer recognisable." From the ophthalmoscopic examination of one case Laqueur also inclined to the view that the bone arose in the choriocapillaris. Knapp, however, obviously went too far when he asserted that the formation of bone in the eye arises exclusively in the capillary layer of the choroid or inflammatory products derived from it, and when he denies the occurrence of true

bone in other parts, such as the lens, retina, and vitreous body. Bone in the lens does occur; in fact, bone-formation has been reported in every tissue of the eye except the cornea. Moreover, the view of the exclusive origin of bone in the choroid from the choriocapillaris is refuted by the cases recorded by Fontan, Schiess-Gemuseus, Brailey, and others, in which the bone was found on the inner surface of the intact membrane of Bruch. Lagrange recognises this alternative situation of the bone, observing that the commencement of the ossifying process may take place between the retina and the lamina vitrea, or external to the lamina vitrea, *i.e.* in the choriocapillaris itself. The latter case, he thinks, is the more frequent, and he explains the former on the ground that the inflammatory exudation from the choroid has



FIG. 356.—BONE IN THE CHOROID. $\times 55$.

From the same specimen as Fig. 355, showing true bone medulla with fat.

early ruptured the lamina vitrea, and spread between this lamina and the retina, and that in this place it is invaded by the process of ossification.

Brailey recorded a number of cases from which he concluded that the bone lies most frequently internal to Bruch's membrane. Fontan and Schiess-Gemuseus record similar cases. The number of Brailey's cases in which the bone lay internal to the vitreous lamina, compared to those where it was situated in the choriocapillaris, is remarkable, considering the total number of cases of ossification of the choroid recorded and the comparatively few cases similar to his that have been elsewhere described. A number of the latter are described in the museum catalogue of Moorfields Hospital, and here support is given to Brailey's view. Various explanations have been put forward as to the origin of the bone in this situation. In some of his cases Brailey traced

its source to the retinal epithelium. This theory is, however, untenable, for it is hardly conceivable that this layer, which is epiblastic in origin, could give rise to a mesoblastic tissue such as bone. Treacher Collins traces the formation of bone inside the membrane of Bruch to an ossification of the hyaline exudation or secretion from the retinal pigment; but it is possible that this hyaline secretion is really mistaken for the clear homogeneous "osteoid" stage of the fibrous tissue as it is being converted into bone. Moreover, for the ossification of this hyaline secretion the cellular or vascular elements must ultimately come from the choroid (Snowball). The more recent researches of Krückmann into the behaviour of the retinal epithelium under pathological conditions seem to oppose the idea that this layer ever takes any real part in the process of ossification.

Alt, again, considers the "colloid bodies" the most frequent source of bone inside the membrane of Bruch. In one of Snowball's cases (No. 5), where ossification is taking place in these bodies, it is apparently independent of that in the other parts of the choroid (in which the bone-formation is more advanced), and is proceeding from the choroidal layers external to these bodies (Fig. 348).

Others, again, believe that the initial changes take place in the vitreous lamina itself.

Cartilage, as an intermediate stage in bone-formation, has been described in cyclitic membrane (Sgrosso), in the choroid (Pes), and in a detached retina (Moauero). It is possible that hyaline deposits containing osteoblasts have been mistaken for true cartilage.

SCHON.—*Ann. d'Oc.*, i, 1838. ARLT.—*Prager Vierteljahrsschrift*, iv, 1847. HULKE.—*Med. Times and Gaz.*, 1857. FÖRSTER.—*Atlas der path. Anat.*, xxxv. PAGENSTECHER.—*A. f. O.*, vii, 1, 1860. KNAPP.—*A. of O.*, ii, 1871. BERTHOLD.—*A. f. O.*, xvii, 1, 1871. SCHIESS-GEMUSEUS.—*A. f. O.*, xix, 1, 1873. LAQUEUR.—*A. f. A.*, vi, 1, 1876. ALT.—*Lectures on the Human Eye*, New York, 1880. GOLDZIEHER.—*A. of O.*, ix, 1880. BRAILEY AND LOBO.—*R. L. O. H. Rep.*, x, 1882. HOENE.—*Rec. d'O.*, 1882. FONTAN.—*Rec. d'O.*, 1883. PARISOTTI.—*Rec. d'O.*, 1887. MEIGHAN.—*Glasgow Med. Jl.*, 1888. REID.—*Glasgow Med. Jl.*, 1888. WHITING.—*A. of O.*, xix, 1888. WOOD.—*A. of O.*, xix, 1888. GROSSMANN.—*A. d'O.*, ix, 1889. GRANDCLÉMENT.—*Lyon Méd.*, 1898. RUIZ.—*Rec. d'O.*, 1899. WEBSTER.—*A. of O.*, xxx, 1901. LAGRANGE.—*Tumeurs de l'Œil*, i, Paris, 1901. MILLIKIN AND DARBY.—*T. Am. O. S.*, 1902. BUCHANAN.—*T. O. S.*, xxiii, 1903. SGROSSO.—*Riforma Medica*, 1890. MOAUERO.—*Ann. di Ott.*, xx, 1891. PES.—*A. f. A.*, xlviii, 1903. *SNOWBALL.—*T. O. S.*, xxiii, 1903 (Bibliography).

TUMOURS

* DERMOID

There is no inherent improbability of a dermoid or other teratoid growth occurring in the choroid. Only one such tumour has, however, been reported. Follin (1861) described a dermoid between the retina and choroid in a woman *æt.* 70. It was composed of dense connective tissue with fat cells, covered with epithelium containing hair-follicles and hairs on the outer side.

FOLLIN.—*Bull. de la Soc. de Chirurgie*, ii, 1861; in Lagrange, *Tumeurs de l'Œil*, i, Paris, 1901.

MYOMA

One case alone of myoma of the choroid has been reported, and that involved the ciliary body. In any case myoma of the choroid can only arise from the posterior prolongations of the ciliary muscle, which are known to stretch far back towards the equator; isolated patches of unstriated muscle have been described in this situation separated from the ciliary body by a portion of normal choroid (Weiss). Guaita's case as much merits being described as a ciliary body tumour as a choroidal, and the diagnosis from a spindle-celled sarcoma rests on the same uncertain grounds as myoma of the ciliary body (q. v.). Indeed, there are cases of such sarcomata of the choroid which much resemble in structure unstriated muscle tissue (*cf.* Panas and Rochon-Duvigneaud).

WEISS.—Nagel's Beobachtungen a. d. ophth. Klinik, Tübingen, i, 3, 1882. GUAITA.—Ann. di Ott., xxiv, 1895. PANAS AND ROCHON-DUVIGNEAUD.—Recherches anat. et clin. sur le Glaucome et les Néoplasmes intraoculaires, Paris, 1898.

ANGIOMA

Angioma of the choroid, which is very rare, must not be confused with angiosarcoma; the latter disease is less rare, and is characterised by its malignancy (*see* "Sarcoma of the Choroid"). An angiomatous condition is seen normally in the rete mirabile of teleostean fishes. Telangiectases of the skin have, in several cases, been associated with extreme tortuosity of the retinal vessels, but in some cases there has been a cavernous angioma of the choroid (Milles, Wagenmann). Other angiomata of the choroid, usually cavernous, have been recorded by Panas and Remy, Lawford (Fig. 357), Nordenson, Schiess-Gemuseus, Giulini, Tailor, Deyl, Steffens, and Greeff. The age of the patient has varied from 5 to 69 years, though the condition is really congenital; in several cases detachment of the retina has occurred, followed by secondary glaucoma.

The tumour usually occurs in the posterior part of the choroid, and is flat or lens-shaped; it has no capsule, but fades off imperceptibly into the surrounding normal choroid, or there may be some aggregation of chromatophores at the periphery. In Wagenmann's case the growth filled the posterior part of the globe; in this, and in Nordenson's case, the inner surface was covered with a layer of bone: neither of these cases were, therefore, simple angiomata, and they may have been osteosarcomata, but such conditions are too rare to admit of dogmatic diagnosis.

The minute structure is that of an ordinary cavernous angioma, and displays much the same varieties. There are large irregular spaces, lined with endothelium, and filled with blood, separated from one another by delicate fibrous walls (Fig. 357). Arteries and veins may be distinguishable in the midst, and parts may be composed of dilated capillaries (telangiectases). Sometimes the fibrous tissue is more

abundant both in the walls of the spaces and upon the surface; in the latter situation it resembles that found not infrequently upon sarcomata and carcinomata, and is probably due to irritative reaction on the part of the stroma. This may possibly account for the bone formation occurring here in Nordenson's and Wagenmann's cases. Scattered chromatophores in the fibrous tissue point to its origin in the choroidal stroma. More cellular parts occur, pervaded with embryonic spindle-cells, as in Nordenson's case; it is impossible to decide on histological grounds alone whether these cells are merely new-formed connective-tissue or sarcomatous cells.

Deyl's case offers some peculiarities. In a child, *æt.* 5, the choroid



FIG. 357.—CAVERNOUS ANGIOMA OF THE CHOROID. $\times 110$.

Lawford, T. O. S., v. Through the thickest part of the growth; note the typical structure, and compare with Fig. 61, Vol. I.

under the macula was occupied by a network of thin-walled, dilated vessels, amid which the thicker-walled ciliary vessels could be seen. The condition was, therefore, telangiectatic, and Deyl adduces it as an explanation of the so-called macular coloboma.

Angiomata apparently occur at any part of the choroid; in only two cases are they definitely stated to have been in the lower quadrant, so that they have no uniform relationship with the fœtal choroidal cleft. Lindsay Johnson, on theoretical grounds, considers that extra-papillary colobomata of the choroid are due to an angiomatous malformation.

PANAS AND REMY.—*Anat. path. de l'Œil*, 1879. PANAS.—*Traité des Maladies des Yeux*, Paris, 1894. MILLES.—T. O. S., iv, 1884. LAWFORD.—T. O. S., v, 1885. NORDENSON.—A. f. O., xxxi, 4, 1885. SCHIESS-GEMUSEUS.—A. f. O., xxxiv, 3, 1888. GIULINI.—

A. f. O., xxxvi, 4, 1890. TAILOR.—Ann. di Ott., xxiii, 1894. DEYL.—Wiener klin. Rundschau, 1899. WAGENMANN.—A. f. O., li, 3, 1900; B. d. o. G., 1903. STEFFENS.—K. M. f. A., xl, 1902. GREEFF.—In Orth, Lehrbuch, Berlin, 1903. LINDSAY JOHNSON.—A. of O., xix, 1890. BELTMAN.—A. f. O., lix, 3, 1904.

PLEXIFORM NEUROMA

Treacher Collins has recently found the choroid affected with neurofibromatosis in cases where this disease is extensive: he has examined two such cases (Snell's, and Rayner Batten's); in both the eyes were buphthalmic. The choroid was considerably thickened, and denser than normal, due to an abnormal overgrowth of its fibrous tissue

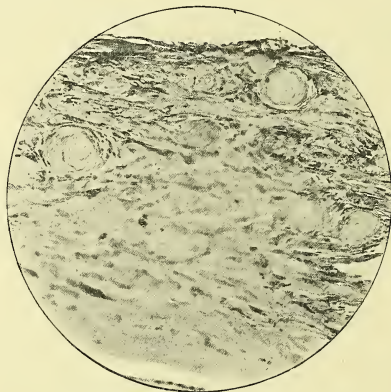


FIG. 358.—PLEXIFORM NEUROMA. $\times 90$.

From a specimen by Treacher Collins. Bodies resembling end-organs in the choroid in a case of plexiform neuroma of the orbit (Treacher Collins and Batten, T. O. S., xxv.)

elements. The fibrous tissue was arranged in layers, and was highly nucleated. Scattered throughout the thickened tissue were an abnormal number of deeply pigmented cells. The blood-vessels seemed few in number, and formed a very much less conspicuous constituent than in normal eyes. In Rayner Batten's case there were present in the hypertrophied tissue numerous sections of small oval bodies, with a nucleated cellular capsule and a core consisting of a convoluted fibre (Fig. 358). These are exactly similar to the bodies resembling nerve endings which I have described in Rockliffe's case of orbital plexiform neuroma (*v. infra*).

SNELL AND TREACHER COLLINS.—T. O. S., xxiii, 1903. *TREACHER COLLINS AND RAYNER BATTEN.—T. O. S., xxv, 1905. PARSONS AND ROCKLIFFE.—Trans. Path. Soc., iv, 1904.

SARCOMA

The earliest clear reference that we have to intra-ocular sarcoma is the discussion which arose upon the subject of pigmentation. Laennec (1819) first drew attention to this peculiarity as a means of classification and nomenclature, since he called the pigmented growths "melanoses." Thence arose a doubt as to their benign or malignant nature, Lawrence (1845), Taignot (1853), and others regarding them as malignant, whilst Sichel (1851) distinguished between benign and malignant melanosis. Virchow (1863), in his immortal treatise, laid the foundations of a rational classification. He distinguished between simple melanomata, melanosarcomata, and melanocarcinomata, and laid stress upon the fact that pigmentation was of secondary importance, the real test being the histological structure of the growths. Virchow himself investigated a series of tumours from v. Graefe's clinic. In 1868 v. Graefe and Knapp simultaneously published clear and accurate accounts of the clinical course of these intra-ocular tumours, bringing forward the essential features, which have only since been modified in comparatively unimportant details. Many isolated contributions to the subject were made in the succeeding years by Hirschberg, Nettleship, Spencer Watson, Argyll Robertson, O. Becker, and others. All the previous work was collated and critically examined, with the addition of 22 new cases—259 in all—by Fuchs, in 1882, in his admirable monograph upon "Sarcoma of the Uveal Tract." In 1891 Lawford and Treacher Collins collected 103 cases from the records of the Moorfields Eye Hospital. In 1898 Leber and Krahnstöver made an important contribution to the subject, collecting and criticising all those cases in which sarcoma of the choroid was associated with phthisis bulbi. In the same year Panas and Rochon-Duvigneaud published their anatomical and clinical researches on "Glaucoma and Intra-ocular Neoplasms." Pawel, in 1899, published reports of 100 cases from the clinic at Halle, and in 1900 Madame Putiata Kerschbaumer wrote a monograph on 67 cases of sarcoma of the eye from the Leipzig clinic. The most recent treatise upon the subject is contained in Lagrange's "Tumours of the Eye" (1901).

Besides these more comprehensive monographs many isolated communications have been published, the most important of which will be referred to.

LAENNEC.—*De l'Auscultation*, etc., Paris, 1819. LAWRENCE.—*London Med. Gaz.*, 1845. Taignot.—*Ann. d'Oc.*, xxix, 1853. SICHEL.—*Ann. d'Oc.*, xxvi, 1851. VIRCHOW.—*Die krankhaften Geschwülste*, Berlin, 1863. v. GRAEFE.—*A. f. O.*, xiv, 2, 1868. KNAPP.—*Die intraocularen Geschwülste*, Carlsruhe, 1868. HIRSCHBERG.—*K. M. f. A.*, vi, 1868; vii, 1869; *A. f. O.*, xiv, 3, 1868; xvi, 1, 1870; xxii, 1, 1876; *A. f. A.*, viii, 1879; ix, x, 1880; *Berliner klin. Woch.*, 1904. NETTLESHIP.—*R. L. O. H. Rep.*, vii, 3, 1872; viii, 2, 1875; ix, 1, 1876. SPENCER WATSON.—*Brit. Med. J.*, 1877. ARGYLL ROBERTSON.—*Edin. Med. J.*, 1877. *FUCHS.—*Das Sarcom des Uvealtractus*, Wien, 1882. LAWFORD AND TREACHER COLLINS.—*R. L. O. H. Rep.*, xiii, 2, 1891. LEBER AND KRAHNSTÖVER.—*A. f. O.*, xlv, 1 and 2, 1898. PANAS AND ROCHON-DUVIGNEAUD.—*Recherches anat. et clin. sur le Glaucome et les Néoplasmes intraoculaires*, Paris, 1898. PAWEL.—*A. f. O.*, xlix, 1, 1900. *KERSCHBAUMER.—*Das Sarcom des Auges*, Wiesbaden, 1900. *LAGRANGE.—*Tumeurs de l'Œil*, i, Paris, 1901.

Classification.—No classification of sarcoma of the choroid is

altogether satisfactory. The old division into melanotic and leucosarcomata, founded upon the presence or absence of pigment, still persists, though it is often scientifically inaccurate, or at least ambiguous (*v. infra*). They may be divided according to form into *circumscribed* and *diffuse, flat* or *infiltrating* (Flächensarcom, tumeur en nappe). There are various classifications founded upon minute structure, the most satisfactory criterion, as shown by Virchow, but by no means easy in practice. Fuchs describes (1) spindle- and round-celled sarcoma, (2) sarcoma with areolar pigmentation, (3) endothelial sarcoma, (4) cavernous sarcoma, (5) fibrosarcoma, (6) alveolar sarcoma, (7) sarcoma combined with glioma, (8) sarcoma combined with tubercle, (9) inflammatory sarcoma with cholesterolin etc., (10) giant-celled sarcoma, (11) myxosarcoma, (12) chondrosarcoma, (13) osteosarcoma, (14) myosarcoma, cystic sarcoma. Kerschbaumer describes (1) angiosarcoma, (2) melanotic sarcoma, (3) leucosarcoma with hæmatogenous pigmentation, (4) spindle-celled sarcoma, (5) combined tumours, (6) degenerating sarcoma. Lagrange divides sarcomata of the uveal tract into melanotic and leucosarcomata, with three subdivisions according to (1) form of the cells, round-celled or encephaloid, spindle-celled or fibrosarcoma, and giant-celled; (2) endothelial origin and grouping of the cells, hæmangiosarcoma, lymphangiosarcoma, alveolar, and tubular; (3) state of the vessels, telangiectatic and cavernous.

In the present state of absolute ignorance as to the ætiology of sarcomata it is wisest to abstain from elaborate attempts at classification, and to use for the present the terms which are universally accepted and understood.

Frequency.—Sarcoma of the uveal tract is rare. Fuchs collected 91 cases in 137,545 eye patients, or 0.066 per cent.; Pawel, 248 cases in 351,779, or 0.07 per cent.

As regards *distribution in the uveal tract* Fuchs found—

Sarcoma of the iris	16		6 per cent.
„ „ ciliary body	22		9 „
„ „ choroid	221		85 „
	259		100

Kerschbaumer found 7 diffuse, 9 epibulbar, 2 iris, 8 ciliary body, 41 choroid; total, 67. Lawford and Treacher Collins found 1 iris, 6 ciliary body, 2 ciliary body and choroid, 94 choroid; total, 103.

These numbers are subject to the criticism that in advanced cases it is impossible to be certain of the site of origin; this applies with especial force to the ciliary body.

With regard to the *eye affected* the results are:

	Fuchs.	Lawford and Collins.	Pawel.
Right eye	108	 41	 43
Left eye. . . .	101	 60	 48
Bilateral	5	 —	 —
Unknown	45	 2	 9
	259	103	100

As regards *age* the results are :

	Fuchs.	Lawford and Collins.	Pawel.
I-10	11	—	1
11-20	16	3	1
21-30	19	7	13
31-40	43	19	11
41-50	55	27	19
51-60	55	22	33
61-70	25	16	18
71-80	10	8	2
81-90	—	1	—
Unknown	25	—	2
	259	103	100
Average	44·2 p.c.	48·42 p.c.	48·7 p.c.

As regards *sex* the results are :

	Fuchs.	Lawford and Collins.	Pawel.
Men	137	59	47
Women	116	44	53
Unknown	6	—	—
	259	103	100

As regards *pigmentation* the results are :

	Iris.		Ciliary body.		Choroid.	
	Pig-mented.	Non-pig-mented.	Pig-mented.	Non-pig-mented.	Pig-mented.	Non-pig-mented.
Fuchs	13	3	20	2	196	25
Pawel	1	1	6	4	39	8

Fuchs' figures work out at 88 per cent. melanotic, 22 per cent. non-pigmented, the latter being commoner in the anterior part of the uveal tract. Pawel's non-pigmented cases include slightly pigmented ones, and agree both as to percentages and site with Fuchs'. In neither case are they very reliable, owing to the confusion of autochthonous and hæmatogenous pigmentation. In this respect Kerschbaumer's results are the best available. She found 13 (19·4 per cent.) melanotic, 27 (40·3 per cent.) non-pigmented, and 27 (40·3 per cent.) non-pigmented but with hæmatogenous pigmentation, a very different result from the other authors. The 13 melanotic sarcomata were: 2 epibulbar, 3 ciliary body, 8 choroid (1 equator, 4 posterior pole, 3 unknown). The 27 leucosarcomata were: 2 diffuse, 5 epibulbar, 2 ciliary body, 18 choroid (1 equator, 14 posterior pole, 3 unknown). The 27 leucosarcomata with hæmatogenous pigmentation were: 5 diffuse, 2 epibulbar, 2 iris, 3 ciliary body, 15 choroid (5 equator, 10 posterior pole).

As regards *histological structure* Fuchs found 62 spindle-celled, 39 round-celled in 229 melanotic; 13 spindle-celled, 12 round-celled in 30 leucosarcomata. Pawel found 30 spindle-celled, 8 round-celled in

88 melanotic, and 2 of each in the 5 pure leucosarcomata. He draws attention to the youth of the patients with non-pigmented growths, average 34·6 years, as against 49·4 years for the melanotic alone; moreover, 3 of the 5 were under 30 years of age. Of all sarcomata of the choroid alone Fuchs found spindle-celled 65, round-celled 40, mixed spindle- and round-celled 28, fibrosarcoma 8, myxosarcoma 3, chondrosarcoma 3 (total 147). The site of the choroidal tumours was— anterior part 14, equatorial 12, posterior part 74, unknown 121 (total

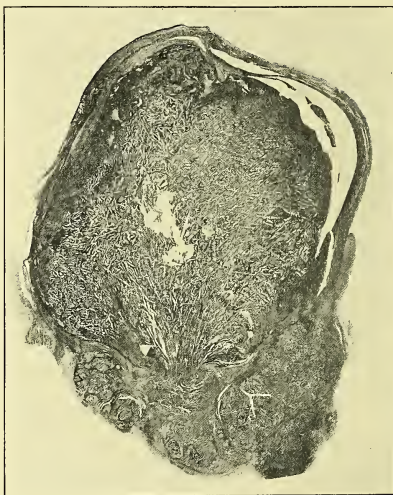


FIG. 359.—SARCOMA OF THE CHOROID. $\times 24$.

From a man, æt. 45. Melanotic sarcoma of the choroid filling the globe and extending into the orbit. (See Parsons, T. O. S., xxv.)

221): 18 of these were external, 17 internal, 7 above, 5 below, 11 in intermediate meridians (total 58).

Ætiology.—It is no part of this work to enter into details as to ætiology, clinical course, etc., but the more important facts serve to throw light upon pathogenesis, and are worthy of brief mention. Fuchs and Pawel, Kerschbaumer, and most other authors have been unable to trace any *hereditary influence*. The following, however, is a remarkable example. A woman, æt. 38, stated that her mother's father was supposed to have lost an eye. The mother, at the age of 38, had her left eye removed for a spindle-celled pigmented sarcoma of the choroid (see Lawford and Collins, 'R. L. O. H. Rep.,' vii, p. 389;

ix, p. 42; xiii, p. 117, case 2). The mother's twin sister had an eye removed. Another sister died at the age of 40 of "tumours" of the breast. Another sister is dead. The patient has 4 older sisters and 1 brother healthy. A younger sister was born a year before her mother's eye was removed, at a time when the latter was undoubtedly suffering from sarcoma of the choroid. This sister's left eye was removed for a pigmented, mixed, round, and spindle-celled sarcoma of the choroid during her first pregnancy (*see* Lawford and Treacher Collins, 'R. L. O. H. Rep.,' xiii, p. 163, case 99). The patient had her breast removed for a tumour nine years ago. A few months later she had great pain in the left eye, which was removed four months

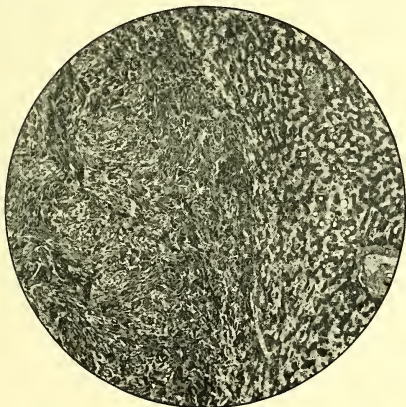


FIG. 360.—METASTASIS IN LIVER. $\times 60$.

From the same specimen as Fig. 359. The patient died a year later, and was found to have sarcoma of the liver and carcinoma of the ribs and lung. The figure shows spindle-celled sarcoma to the left, normal liver to the right. (*See* Parsons, T. O. S., xxv.)

afterwards. Her right eye was recently removed; I examined it, and found a large melanotic sarcoma involving the ciliary body and choroid (*see* Parsons, 'T. O. S.,' xxv).

Lawford and Collins report 14 cases in which near relatives had "tumours."

Cases of sarcoma of the eye, associated with carcinoma elsewhere, have been reported (Fisher and Box, Parsons). The case which I have reported is absolutely unequivocal. A melanotic sarcoma of the choroid in the third stage (Fig. 359), with an unpigmented extra-ocular extension, was associated with bile-stained, unpigmented spindle-celled sarcoma of the liver (Fig. 360), and squamous-celled carcinoma of the ribs (Fig. 361), lung, and mediastinal glands. The occurrence is

probably fortuitous, neither growth having any causal relationship to the other, though both may be due to some underlying predisposition.

There was a history of *injury* in 29 of Fuchs' cases (11 per cent.), and in 5 of Lawford and Collins'; there is no sufficient evidence that it is of ætiological moment. There is rather more evidence in favour of prolonged *inflammation* (Virchow, Leber and Krahnstöver, Pawel), but analysis of the cases in which the conditions are combined tends to minimise its importance (*v. infra*). Statistics as regards *age* and *sex* have already been given and speak for themselves.

Course.—Sarcoma of the choroid passes through the four stages characteristic of all intra-ocular malignant growths—(1) the pre-glaucomatous stage; (2) secondary glaucoma; (3) extra-ocular extension; (4)



FIG. 361.—CARCINOMA OF RIB. $\times 120$.

From the same patient, showing squamous-celled carcinoma of rib. (See Parsons, T. O. S., xxv.)

metastasis. In the first stage the retina is pushed forward and detached. There may also be a simple detachment of the retina in the lower part of the globe, probably caused by increased secretion of fluid by the choroid, due to the irritation set up by the tumour. This fluid gravitates to the lowest part of the globe, and causes detachment, which may be large, even when the tumour is small (Parsons). In most cases the first stage lasts about $\frac{1}{2}$ to 1 year, but may reach several years; average of 67 cases, 21 months (Fuchs).

Secondary glaucoma is induced by several causes, which vary in importance in different cases. The detachment of retina increases, and may become complete, the shrinking vitreous pressing the lens and iris forwards, so that the angle of the anterior chamber becomes blocked. The situation of the tumour is of importance, for it may be

such as to obstruct the exit of blood by the veins. The angle of the anterior chamber not uncommonly becomes partially blocked by pigmented cells. Less frequently plastic irido-cyclitis is set up, bringing increased tension in its train; these eyes may go on to phthisis bulbi (*v. infra*). Glaucoma may be precipitated by the use of mydriatics. The second stage is usually shorter than the first—generally less than one year.

Extra-bulbar extension of the growth takes place along the perforating vessels—anterior, equatorial, or posterior—or by way of the optic nerve. The neighbouring sclerotic is rapidly destroyed, and the tension is relieved. If perforation occurs along the anterior ciliary vessels, the extra-ocular growth, which is so often melanotic, is readily diagnosed. In the other cases exophthalmos subsequently sets in, rarely masked by coincident shrinking of the globe. It may be eccentric, according to the site of perforation. The extra-bulbar tumour grows with increased rapidity, owing to diminished resistance, and may rapidly fungate and ulcerate. Kerschbaumer examined 23 cases (out of 58), with extra-ocular extension; it occurred in 6 out of 7 diffuse sarcomata, in 5 out of 8 of the ciliary body, in 2 out of 2 of the iris, and in 10 out of 41 of the choroid; 10 perforated in the posterior part of the globe, 3 in the equator, 6 in the anterior part, and in 4 the site could no longer be determined.

Extra-ocular extension occurs also along the ciliary nerves, but this is much less common than along the perforating vessels.

Metastasis may occur early, and is common after excision during the first stage. It takes place by way of the blood-vessels, and probably varies with the disposition of the vessels in the growth rather than with its cytological character. Of 21 cases in which death resulted from metastasis, the cells were spindle-shaped in 8, oval in 1, round in 5, mixed in 5, and not noted in 2 (Lawford and Collins). Metastases usually occur first in the liver, then in the lungs, then in other organs. Fuchs gives the following order of frequency: liver, 3; stomach, 7; subcutaneous tissue, 4; heart, kidney, bones, serous membranes, 3; lungs, 3; vertebral column, lymphatic glands, 2; spleen, pancreas, intestine, epiglottis, brain, each 1. The pre-auricular and neighbouring glands are almost never affected. Local metastasis in the eye itself is very rare, so that sarcoma of the uveal tract differs totally in this respect from glioma retinae. Knapp describes a case in which there was a melanotic sarcoma of the choroid, and smaller nodules between the choriocapillaris and the pigment epithelium, as well as on the back of the completely detached retina. He considers that these were deposited by continuity whilst the retina was still *in situ*. Mitvalski also describes secondary nodules in the retina. Ewetzki found tumour-cells in the vitreous and a small nodule in the retina in a case of sarcoma of the iris. Where there are apparently isolated growths continuity can usually be made out microscopically, though the cells in the intermediate area may be degenerate (Mitvalski). Microscopic nodules of cells may lift up the pigment epithelium at spots around the growth, and not in direct continuity with it. These are regarded by Bruns and Leber as local metastases. Pigmented cells are often carried

into the vitreous and other parts of the eye, frequently accumulating in the angle of the anterior chamber (Panas and Rochon-Duvigneau, Ewetzki, and others). These rarely, if ever, lead to true metastatic deposits; they remain inert, apart from the obstruction which they cause to the normal outflow of lymph from the eye.

Metastases are much more frequently the cause of death than local recurrence, thus again differing from glioma retinae. Out of 243 cases, death was due to generalisation in 45 (18½ per cent.) (Fuchs); this is doubtless much too low a computation. In 3 cases which refused operation the total duration of the disease was 5½, 3¾, and 1¾ years respectively. In 89 cases of sarcoma of the choroid and ciliary body local recurrence occurred in 9 (Pawel), 8 being before the end of the second year after operation. Lawford and Collins traced 79 cases, of whom 40 were dead; 20 of the remaining 39 were alive three or more years after removal of the primary growth (25 per cent.). In 26 cases death was due to metastasis or recurrence, and the average duration of life was 2 years and 4 months. In 7 there was local recurrence, 6 within seven months. I have notes of a case in which Lawford removed an eye with very extensive extra-bulbar growth; local recurrence took place, and the orbit was exenterated: the patient was alive and well seven years subsequently.

Extra-ocular extensions often show differences of structure from the intra-ocular growths. There is frequently a pseudo-alveolar arrangement, due to infiltration of the pre-existing tissue spaces in the capsule of Tenon, etc. The extra-ocular growth is often non-pigmented when the intra-ocular tumour is melanotic, and the same is true of the general metastatic deposits. Thus some secondary nodules in the liver may be pigmented, whilst others are free from pigment. Pigmented metastases from primary leucosarcomata do not seem to occur (Fuchs). The form of the cells may differ from those in the eye; thus, with a primary spindle-celled sarcoma, round cells may prevail in the metastases and *vice versa*. Specialised structure, present only in parts of the primary growth, may be universal in the secondary deposits, *e.g.* an alveolar structure.

Metastasis by the blood-vessels is facilitated by the frequency of wall-less channels in the primary growth. The normal blood-vessels of the eye may also be actually invaded by the tumour-cells with the formation of intra-vascular thrombi. This occurs especially in the venae vorticosae, but is relatively rare. It is easy to understand how malignant emboli may get free in the general circulation under these circumstances. They are most likely to be filtered off in the small capillaries of the liver, and it is here, as we have seen, that metastatic deposits are most common.

WILLIAMS AND KNAPP.—A. f. A., iv, 1874. MITVALSKI.—A. f. A., xxviii, 1894. MARSHALL.—T. O. S., xvi, 1896. EWETZKI.—A. f. O., xlii, 1, 1896. KAMOCKI.—Z. f. A., iii, 1900. FISHER AND BOX.—T. O. S., xx, 1900. *PARSONS.—T. O. S., xxv, 1905; Ophth. Rev., xxiv, 1905. BRUNS AND LEBER.—A. f. O., liv, 3, 1902. BIRNBACHER.—Hirschberg's Festschrift, 1905.

Macroscopic appearances.—As already mentioned, there are two types of sarcoma of the uveal tract, the circumscribed and the diffuse. Of these the latter is extremely rare, and will receive separate con-

sideration; in their mode of infiltration they resemble metastatic carcinoma. Circumscribed sarcoma of the choroid, when small, is lenticular in shape; later it becomes mushroom-shaped.

The shape of these tumours is more important than might appear at first sight, since it indicates fundamental differences of origin and growth. The ordinary primary sarcoma starts in the actual stroma cells of the choroid itself. Following the laws of growth, the cells proliferate in the directions of least resistance. Since the growth commences *in* the actual tissues themselves, the resistance is equal in all directions at first, so that at this stage we might expect the tumour to be spherical. Soon, however, the greater resistance on the side of the sclerotic begins to make itself felt, the advance is less in this direction, whilst equal in other directions; hence the tumour becomes roughly elliptical, growing twice as fast laterally as in thickness. This mode of advance continues until the membrana vitrea is burst through, which results from equable stretching rather than from any localised attack by the growth upon any one spot. At the hole in Bruch's membrane, which is necessarily central as to the surface of the tumour, resistance is greatly relieved, proliferation becomes most active in this direction, and a new focus is established in the subretinal space. Here again resistances are equalised, growth proceeds equally in all directions, and the very characteristic globular head of the tumour is formed, connected with the main mass by a short neck at the level of Bruch's membrane (Figs. 362, 363).

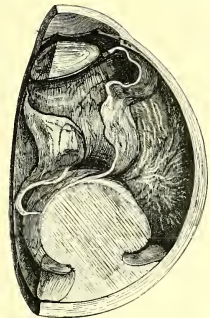


FIG. 362.—SARCOMA OF THE CHOROID.

R. L. O. H. Museum. Typical mushroom shape.

These essential tendencies of growth may be modified in detail in different cases, *e. g.* by proximity to a vorticosc vein, so that a new path of diminished resistance is afforded. I have recently seen a unique sarcoma of the choroid resembling clinically a ciliary staphyloma (Arnold Lawson and Parsons). The tumour extended from the ciliary body to the optic nerve on the outer side, increasing in thickness posteriorly (Fig. 364). The sclerotic was split, a thin layer covering the growth, whilst islets of sclerotic were imbedded in the tumour anteriorly. The retina was *in situ*. The growth probably started near a vortex vein, and invaded the interlamellar spaces of the sclerotic.

Cytology.—Virchow first pointed out that the cell-form in sarcomata of the eye is of greater importance than pigmentation. For accurate determination of cell-form teased preparations are best, and it is to be regretted that this serviceable method has largely fallen into disuse. Errors are liable to arise from deductions based upon sections alone: when these are thick the shape of the cells is obscured by their multiplicity; when they are thin portions only of the larger cells are seen. Many tumours described as mixed round and spindle-celled are in

reality pure spindle-celled, the appearance of round cells being given by transverse section of bundles of spindle-cells. This error can usually



FIG. 363.—SARCOMA OF THE CHOROID. $\times 9$.

Early melanotic sarcoma in the macular region, showing typical mushroom shape. The broken ends of the lamina vitrea are curled up at the edge of the neck.



FIG. 364.—ATYPICAL SARCOMA OF THE CHOROID. $\times 2\frac{1}{4}$.

From a man, æt. 34. Arnold Lawson and Parsons, T.O.S., xxv.

be avoided by noticing that many of these round bodies contain no nuclei, only the peripheral portions of the protoplasm having been cut

across. So, too, cells which appear fusiform in sections are often star-shaped, the processes being numerous, originating in all planes, and by no means always from the poles; such cells have far more resemblance to the normal chromatophores than the appearances in sections would lead one to expect (Ribbert).

The so-called spindle-celled sarcomata are by far the most common in the uveal tract, forming about half the total number of cases. The cells vary in size, and much resemble embryonic connective-tissue cells, having a large oval nucleus with ample chromatin and one or more large nucleoli, and a fusiform cell body, the ends of which often bifurcate. The cells are usually closely packed together, forming bundles which cross in various directions and interlace. According to Ackermann the cells are not round but flattened, the nuclear part being rather thickened, whilst the processes are ribbon-like bands. There is usually little or no stroma.

Round cells are frequently so called from the shape of their nuclei rather than that of their protoplasm. The small "round" cells are generally irregular in shape, and often have short processes, thus differing from lymphocytes and the cells of lymphomata. They show every gradation in size, passing insensibly into the large round cells. These are epithelioid, with oval faintly staining nuclei, containing one or more well-marked nucleoli; the cell body is flat, irregular, and often has processes. When these cells are closely packed they are frequently square or polygonal. The round cells, especially the small type, usually lie in a well-marked reticular stroma. Round-celled sarcomata are commoner in the non-pigmented group, and are derived, according to Knapp, Briere, and Schieck, from the choriocapillaris. This is denied by Fuchs and most other observers, all sarcomata of the choroid originating in the outer layers.

Round-celled sarcomata grow more quickly than the fusiform or mixed: the average duration at the time of operation in Fuchs's cases was 18½ months in round-celled, 30 months in spindle-celled, and 34 months in mixed-celled sarcomata. Recurrence or metastasis occurred in 37 per cent. of the mixed-celled, 29 per cent. of the round-celled, and 19 per cent. of the spindle-celled. Round-celled sarcomata are commoner in the anterior part of the eye than in the posterior (16 cases to 10 round-celled, 23 to 27 spindle-celled, 4 to 9 mixed-celled, Fuchs). They occur in younger subjects (average age—38 round-celled, 45 spindle-celled, 49 mixed-celled, Fuchs).

Giant cells have been described in a few cases (Nettleship, Hirschberg, Poncet). Nettleship's and Hirschberg's cases were children, æt. 14 and 2 respectively; they were probably tubercular. Poncet's case showed advanced degenerative changes and was probably of the same nature. Multinucleated cells are not uncommon in sarcomata, but usually differ much from ordinary giant cells; they are evidence of rapid nuclear division. They frequently contain pigment (Fuchs). Knapp, Michel, Alt, and Jackson have described cartilage in sarcomata of the choroid; this is probably an error of observation.

RIBBERT.—Ziegler's Beiträge, xxiii, 1898. ACKERMANN.—Volkmann's Sammlung, 1883. BRIÈRE.—Thèse de Paris, 1873. SCHIECK.—A. f. O., xlv, 2, 1898; xlviii, 2, 1899.

NETTLESHIP.—R. L. O. H. Rep., viii, 2, 1875. HIRSCHBERG.—A. f. O., xxii, 1, 1876. PONCET.—Atlas de l'Anat. path., 1879. DE LAPPERSONNE AND OPIN.—A. d'O., xxiii, 1903. MICHEL.—A. f. O., xxiv, 1, 1878. FEHR.—C. f. A., xxvii, 1903. ALT.—A. of O., viii, 1879. JACKSON.—T. Am. O. S., 1897. ARNOLD LAWSON AND PARSONS.—T. O. S., xxv, 1905.

Structure.—The structure of sarcomata of the choroid depends chiefly upon the nature and arrangement of the blood-vessels. The tumours are always very vascular. The new formed vessels are simple endothelial tubes, with a very wide lumen (Fig. 365). Other blood-channels are common, possessing no proper wall, bounded only by the cells of the growth; these account for the rapidity of metastasis by means of malignant emboli. The older vessels may develop a scanty connective-tissue sheath, but those possessing well-developed media and adventitia are invariably preformed vessels which have become

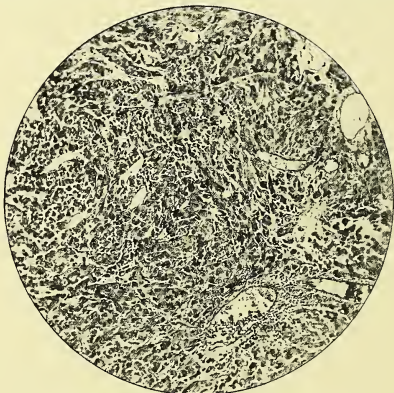


FIG. 365.—SARCOMA OF THE CHOROID. $\times 60$.

Note the numerous thin-walled vessels.

imbedded in the growth. Ordinary sections give but little idea of the vascularity of the tumour, as the channels and capillaries are often empty and may easily pass unnoticed. The wall-less and thin-walled vessels readily lead to extravasations of blood, so that hæmorrhages and the products of degeneration of blood-clots are common. The vessels are arranged quite irregularly in many sarcomata. In young spindle-celled growths the tumour-cells are directed longitudinally to the axis of the new capillaries, and form a sheath; this arrangement is lost in later development (Ackermann). When the distribution of thin-walled vessels and blood-spaces is very pronounced the tumours are sometimes called *telangiectatic* or *cavernous* (Leber, Brailey, Knapp, Fuchs). They do not represent a definite type, but are the ultimate expression of the usual arrangement. Hæmorrhages are particularly common in them, and early metastasis is the rule.

An *alveolar* arrangement is frequent, and may arise from various causes. The normal spaces in the choroid may become filled with tumour-cells, which force apart the fibrous and elastic tissue stroma, giving an appearance of alveoli (*see* "Flat Sarcoma"). This structure is common at the base of many choroidal sarcomata. A more extensive pseudo-alveolation is due to the arrangement of the vessels. These divide dichotomously and anastomose, marking out areas which are occupied by tumour-cells. The latter often appear to have no stroma between them, and this is especially the case in the large round-celled sarcomata. Hence arose the term *sarcoma carcinomatoides* (Virchow) and the description of mixed sarcoma and carcinoma (*v.* Graefe, Landesberg, Derby, Schiess-Gemuseus). Billroth first succeeded in pencilling out the cells of such nodules after hardening in chromic acid; he was thus enabled to demonstrate a fibrous reticulum, and to dispel the idea that they were carcinomatous. It is doubtful, however, if such a reticulum is invariably present, but the origin of the cells from mesoblastic elements—often endothelium—cannot be doubted (*v. infra*). The first tumour of this type was observed by *v.* Graefe and examined by Virchow. Other cases have been published by Becker, Pagenstecher and Genth, Alt, Knies, Fuchs, and others, and the subject has been reviewed by Neese.

In some cases the cells are arranged very regularly in layers around thin-walled vessels, so that a *tubular* structure is seen; these form a group of the so-called *angiosarcomata*. In sections they show a superficial resemblance to glioma retinae. Such cases have been described by Günther, Panas and Rochon-Duvigneaud, Kerschbaumer, etc. In Nettleship's case, which I had the opportunity of examining, the eye had been blind for many years, the patient being 24 years old: detachment of the retina had been diagnosed shortly after the defect in vision was noticed. To the naked eye there was a solid brown mass on the temporal side, which showed numerous relatively large spaces (Fig. 366). Microscopically, the tumour was found to consist for the most part of round or round-oval unpigmented sarcoma cells, with medium-sized nuclei and but little protoplasm (Figs. 367, 368); but in some places the cells were spindle-shaped and pigmented. The greater part was permeated by wide blood-spaces (Fig. 369, *b*), and these were separated from the tumour-cells by only one or two layers of very elongated cells, which, seen edgewise, looked like fibres. The blood-spaces were so numerous as to give the growth an almost cavernous character. Midway between the blood-vessels the tumour cells were larger, containing more protoplasm (Fig. 367), and at the centre of some of these evascular areas were groups of spherical

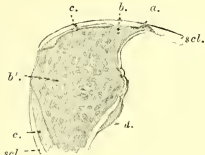


FIG. 366.—SARCOMA OF THE CHOROID.

Nettleship, T. O. S., xxiv. Section of tumour and its coverings, slightly enlarged. *scl.* Sclerotic. *a.* Offshoot from tumour passing almost through sclerotic. *b.* Marginal part of tumour, nearly free from vessels. *b'.* Angiomatic portion of tumour. *c.* Stratum containing cholesterol between tumour and sclerotic. *d.* Fibrous stratum between tumour and retina.

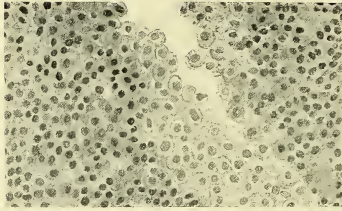


FIG. 367.—SARCOMA OF THE CHOROID. $\times 300$.

From the same specimen, showing the character of the cells which form the chief part of the tumour.

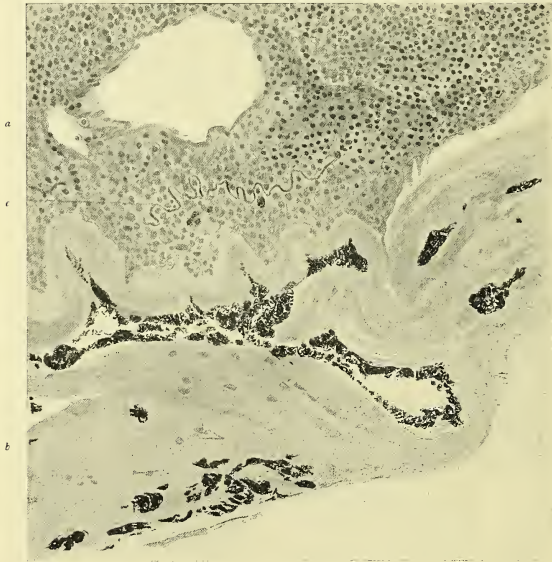


FIG. 368.—SARCOMA OF THE CHOROID. $\times 200$.

From the same specimen, showing the layer of dense fibrous tissue covering the inner—retinal—surface of the tumour. *a*. Tumour cells. *b*. Fibrous layer, enclosing remains of pigmented epithelium. *c*. Lamina elastica of choroid, appearing as a very convoluted, highly refracting line just beneath the surface of the tumour.



FIG. 369.—SARCOMA OF THE CHOROID.

From the same specimen. *a*. Cholesterin-bearing layer of old laminated structure on scleral surface of sarcoma. *b*. The tumour, with numerous blood-spaces. *c*. Situation of sclerotic.

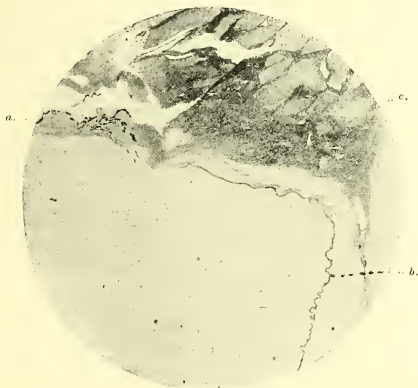


FIG. 370.—SARCOMA OF THE CHOROID.

From the same specimen. *a*. Fibrous stratum on inner surface of growth. *b*. Epithelium- and "colloid"-bearing layer from which *a* appears to have been derived.

pigmented corpuscles; similar pigment masses were also found close to the walls of many of the vessels. The periphery of the base of the tumour, presumably its youngest part, consisted entirely of unpigmented small cells, with but few vessels (Fig. 366, *b*). The tumour was peculiar in that the outer and inner surfaces were covered to a large extent by a stratum totally unlike the main mass, and apparently the result of inflammation, or, perhaps, of copious hæmorrhage, before the sarcoma began.

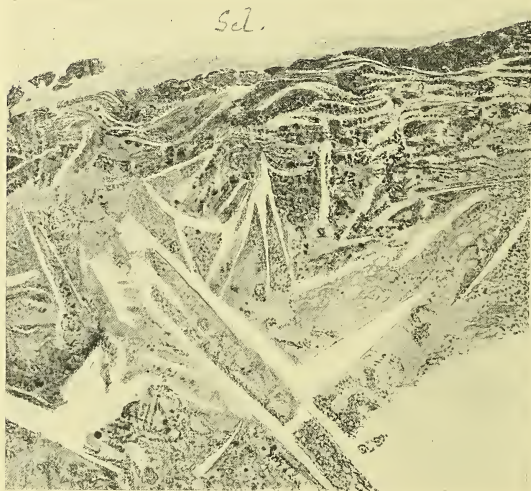


FIG. 371.—SARCOMA OF THE CHOROID. $\times 200$.

From the same specimen, showing a small portion of the layer *a* in Fig. 369 more highly magnified. It contains much brown pigment (from the lamina supra-choroidea), but no nuclei and no blood-vessels. *scl.* Situation of sclerotic, which is thin here but healthy in structure.

Of these two strata, the outer one, lying between the sarcoma and the sclerotic, and sharply marked off from both, was irregularly laminated and permeated by numerous spaces, which had the form of thin, wedge-shaped crystals, and were, no doubt, occupied by cholesterin until the specimen was put into alcohol (Fig. 366, *c*, Fig. 369, *a*, Fig. 371). The layers of this stratum nearest the sclerotic were much pigmented, the remainder less so; the stratum contained no blood-vessels; it covered, in varying thickness, the greater part of the tumour,

being quite absent only over the marginal, comparatively evascular periphery (Fig. 366, *b*), and over the most prominent central part, where the sclerotic was extremely thin and in direct contact with the sarcoma. This cholesterol-bearing stratum varied in thickness from less than 0.5 mm. to fully 2 mm. (Fig. 366).

The other stratum, lying between the sarcoma and the disorganised retina (Fig. 366, *d*), was thinner, less extensive, and had the structure of dense, wavy fibrous tissue, with scattered oval nuclei (Fig. 368, *b*, Fig. 370, *a*); large masses of pigment, the remains of the retinal epithelium, were imprisoned at many places; there were no vessels. This stratum of fibrous tissue extended as a definite structure over, perhaps, one fourth or one third of the surface of the growth, and was thickest—fully 1 mm.—at about the centre; peripherally it passed into a thin, structureless membrane, bearing the pigmented epithelium upon its inner surface (Fig. 370, *b*). This epithelium-bearing membrane was probably the inner part of the membrane of Bruch, for the outer, more elastic part of this membrane could be traced as a very undulating, highly refracting line in the substance of the sarcoma close to its inner surface (Fig. 368); towards the margin of the tumour the two parts of the elastic lamina met, coalesced, and passed on together to the choroid (Fig. 372) (*cf.* Fig. 326).

Kerschbaumer has paid special attention to angiosarcomata of the uveal tract. The term is a somewhat elastic one, and its significance varies with different authors. Lubarsch and v. Hippel divide angiosarcomata into hæmangiosarcoma and lymphangiosarcoma. There are only lymph spaces in the choroid, so that we should not expect true lymphangiosarcoma to occur there (Coppez). Only one such case has been recorded by Lagrange. The patient was a woman, æt. 74; the tumour was mostly non-pigmented, only a small portion near the base being melanotic. It was spongy in texture, and consisted of a network

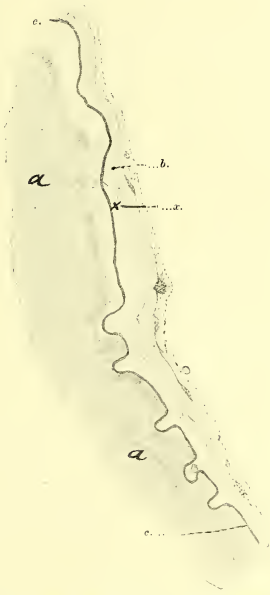


FIG. 372.—SARCOMA OF THE CHOROID.
× 200 circa.

From the same specimen. *a*. Tumour. *b*. Faintly laminated layer (shown also as *b* in Figs. 368 and 370) bearing the pigmented retinal epithelium, here much degenerated on its inner surface. *c*. Lamina elastica, separating *x* from the epithelium-bearing *b*, and becoming attached to the tumour, into which farther on it passes, as shown in Fig. 368.

of cavities, which did not contain blood. The walls were formed of layers of cells of endothelial origin. The blood-vessels formed

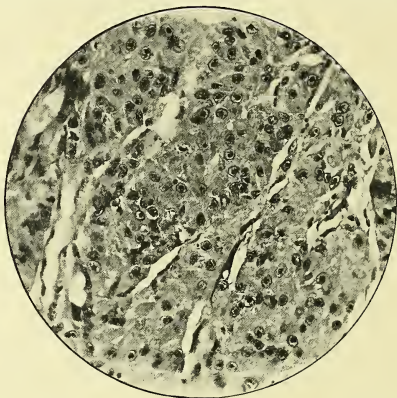


FIG. 373.—MELANOTIC SARCOMA OF CHOROID. $\times 240$.

The growth is an angiosarcoma, composed of cylindrical columns of epithelioid cells; it is probably a perithelioma.



FIG. 374.—SARCOMA OF THE CHOROID.

R. L. O. H. Museum. From a man, æt. 35, showing peculiar foliated arrangement, resembling the convolutions of the brain. (Lawford and Treacher Collins, R. L. O. H. Rep., xiii.)

a separate system. Kerschbaumer regards nearly all hæmangiomata of the eye as perivascular, only a few being intra-vascular (*v. p.*

520). They only occur in the posterior part of the choroid. In 10 out of 11 cases they were associated with disease of the choroidal vessels. They grow slowly, showing few mitoses or multinuclear cells. They commence by hyperplasia of the perithelium of the vessels of Haller's and often of Sattler's layers; in some cases the walls of the capillaries of the choriocapillaris show hyaline thickening. This is also a common feature in the vessels of the growth, and often leads to narrowing or obliteration of the lumina; it may go on to amyloid or myxomatous degeneration (Kerschbaumer). Degeneration is also conspicuous in the peripheral cells of the tubular vessel sheaths, so that the resemblance to glioma retinae is increased. This causes inflammatory reaction in the uveal tract, but whether this is always secondary may be doubted (*cf.* Nettleship's case). Autochthonous pigmentation is the exception in these cases, but hæmatogenous pigmentation is usually a well-marked feature. The stroma often shows extensive degeneration, with the formation of swollen hyaline masses. The cells also swell and degenerate, the nuclei becoming four or five times their normal size, losing their staining power. Wall-less blood-channels do not occur in angiosarcomata (Kerschbaumer).

It should be noted that in none of these types is there a true alveolar structure; the nearest approach to it is found in the filling of preformed lymph-spaces with tumour-cells. This, however, is usually a coincidence of infiltration of normal structures, and not a real characteristic of the tumour growth *per se*.

LEBER.—A. f. O., xiv, 2, 1868. BRAILEY.—R. L. O. H. Rep., viii, 1875-76. KNAPP.—*Loc. cit.*, and T. Am. O. S., 1879. V. GRAEFE.—A. f. O., x, 1, 1864; xii, 2, 1866. LANDESBERG.—A. f. O., xi, 1, 1865. DERBY.—Boston Med. and Surg. J., 1872. SCHIESS-GEMUSEUS.—Virchow's Archiv, lxi, 1876. BECKER.—A. f. A., i, 1872. PAGENSTECHER AND GENTH.—Atlas der path. Anat. d. Auges, Wiesbaden, 1873. ALT.—A. f. A., vi, 1877. KNIES.—A. f. A., vi, 1877. *NEESE.—A. f. O., xliii, 2, 1897. GÜNTHER.—A. f. A., xxv, 1892. HOLDEN.—A. of O., xxi, 1892. PANAS AND ROCHON-DUVIGNEAUD.—*Loc. cit.*, 1898. *NETTLESHIP.—T. O. S., xxiv, 1904. PUSEY.—A. of O., xxxiii, 1904. V. HIPPEL.—Ziegler's Beiträge, xiv. BAQUIS.—Ann. di Ott., xxxiii, 1904.

Pigmentation.—The pigment lies chiefly in cells, less frequently as isolated or clumped granules between the cells (Fig. 375). The distribution is usually irregular, parts of the tumour being melanotic, whilst others are non-pigmented. The difference may be conspicuous, or result only in mottling or areolar pigmentation. The pigment is derived from two sources, from preformed pigment—*autochthonous*, or directly from the blood—*hæmatogenous*. In the former case it may be distributed uniformly or very irregularly, being far from the vessels or situated indifferently with regard to them. In the latter case it generally shows some definite relation to the blood-vessels or to hæmorrhages, being most marked in their immediate vicinity. This is the commonest cause of an areolar arrangement.

Intracellular pigment occurs in many types of cells, which have been well enumerated by Ginsberg.

(a) *Chromatophores.*—These are often massed chiefly near the base and at the periphery of the tumour, or in definite patches. They are then closely packed and deeply pigmented, so that these parts of the

tumour appear coal black to the naked eye. In other cases the chromatophores lie amongst non-pigmented spindle- or star-shaped or round cells. The chromatophores are usually large spindle- or star-shaped cells with long processes. The pigment consists of spherical granules, which are most closely aggregated in the processes and along the periphery of the cells, in accordance with the physiological formation of pigment in chromatophores (Rieke). When densely massed the granules may fill the cytoplasm and obscure the nucleus. The cells are readily bleached—best by permanganate of potassium followed by oxalic acid—and the cells are then seen to possess the typical features of normal uveal chromatophores.

(b) *Transition cells*.—These, according to Ribbert, are contracted

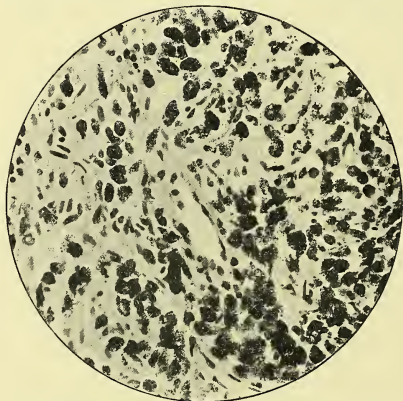


FIG. 375.—MELANOTIC SARCOMA OF CHOROID. $\times 200$.

Deeply pigmented sarcoma; the cells are mostly spindle-shaped; note the round pigment granules.

chromatophores; they also occur in inflammatory conditions in the choroid. They have very short processes, or these may be absent, the cells being irregular or angular. The pigment forms spherules of unequal size, very densely packed. Isolated pigmented cell processes may be seen between the cells in sections, but this is due to the cells being divided.

(c) *Polygonal cells*.—Very large, deeply pigmented, round or polygonal cells are often seen in the blackest parts, usually massed together in large heaps without any apparent relationship to the blood-vessels. The pigment may be uniformly distributed, as if in solution, or may form dark masses. The nuclei are obscured by the pigment, but on bleaching are found to be shrunken and angular, though still staining well with nuclear stains. The cell-body is then seen to be much

swollen, resembling fat cells under a low power. The ease with which they are bleached, the absence of iron reaction, and their disposition irrespective of the blood-vessels, show that the pigment is autochthonous. In form they resemble swollen retinal pigment epithelial cells, such as are found in degenerative conditions (*v. infra*). The absence of rod-shaped pigment granules is not incompatible with this view. Others regard them as chromatophores which have undergone degeneration (Ginsberg). The cells may completely necrose, setting free their pigment and shrunken nuclei, which now pervade a granular necrotic mass. Such a condition is recorded by Ginsberg in a tumour, chiefly non-pigmented, with two intensely pigmented nodules. The periphery of the nodule was black, whilst the centre was chrome yellow, and showed golden masses and granules with sparse nuclear remnants.

(d) *Large round cells*.—These occur in alveolar sarcomata. Most of the cells are non-pigmented, the pigment lying in irregular clumps along the septa, or, on the contrary, far away from them. In either case an alveolar arrangement is seen. Ribbert isolated pigment cells which appeared to be round in section, and found that they were chromatophores. This does not apply to most of the pigment in alveolar sarcomata, which is undoubtedly hæmatogenous.

(e) *Retinal epithelium*.—When the lamina vitrea is perforated the pigmented retinal epithelial cells can invade the growth. They are definitely diagnosed by their pigment, which consists of minute rods, though they may give an iron reaction if there has been hæmorrhage in their neighbourhood (E. v. Hippel, Leber, Lagrange). An analogy for this is found in carcinoma cells containing iron in the liver (Schwalbe). Schieck and Ginsberg regard ingrowth of retinal pigment cells as very rare; Kerschbaumer describes several cases and the occurrence cannot be doubted. Ribbert and Tashiro, however, consider these cells contracted chromatophores.

(f) *Leucocytes*.—Leucocytes containing pigment are found most commonly in the vicinity of hæmorrhages or blood-spaces. They are not so common in sarcomata as larger cells, five or six times the size, which in other respects resemble them. The pigment is often lighter in colour than the autochthonous pigment, but the latter may also be taken up by leucocytes. They may also contain red corpuscles in various stages of degeneration. The pigment usually gives the iron reaction, and is bleached by hydrochloric acid, whilst the ordinary bleaching reagents—bleaching fluid, eau de Javelle, permanganate of potassium and oxalic acid, etc.—have no effect. Some of the pigment withstands the action of hydrochloric acid, as in siderosis bulbi (E. v. Hippel). The pigment granules are usually coarse and irregular; no nucleus may be visible even in lightly pigmented cells. The cells are found mostly in or near blood-spaces and vessels, and the reactions show that most of the pigment is hæmatogenous. They are much commoner in ordinary intra-ocular hæmorrhages than in sarcomata. Schieck suggests that they are sarcoma cells or chromatophores, but some of them are certainly not.

Blood-pigment and rarely hæmatoidin crystals are found as golden or brown clumps near hæmorrhages.

The origin of the pigment in melanotic sarcomata has been much discussed. Two sources have been suggested, viz. preformed pigment (autochthonous), and the hæmoglobin of the blood (hæmatogenous). Autochthonous pigment is a product of the cell metabolism, and only those cells can produce pigment which are the offspring of pigmentiferous cells. This source has been upheld by Virchow, v. Recklinghausen, Waldeyer, Mertsching, Ritter, Ziegler, Fuchs, and others. There are two sets of pigmentiferous cells available. The so-called chromatophores of the choroidal stroma are regarded as the sole source of the cells by Ribbert. The retinal pigment epithelium undoubtedly plays a subsidiary part, and is negligible as an integral factor in pigment production. Langhans and Gussenbauer first asserted a purely hæmic origin for the pigment. This view has been wholly or partially accepted by Vossius, Birnbacher, Oppenheimer, and many more recent observers.

Melanin, the pigment from melanotic sarcomata, has never been obtained pure for analysis. Addition of caustic potash to a melanotic growth turns the pigment bright red; concentrated sulphuric acid causes a play of colours—green, then blue, then red (Virchow). Heintz first attempted the analysis of melanin, and found that it contained carbon, 53·4 per cent.; hydrogen, 4·02 per cent.; nitrogen, 7·10 per cent., and no iron. Dressler found traces of iron. Berdez and Nencki found carbon, hydrogen, oxygen, nitrogen, and as much as 10·67 per cent. of sulphur, but no iron, phosphorus, or chlorine. They called the pigment phymatorusin. The subject was exhaustively investigated by Mörner; both the urine, which often contains the pigment (melanuria), and the tumours were examined. The pigment gave no absorption bands, but was found to contain iron, which was estimated spectrophotometrically. Failure to find iron is due to the use of hydrochloric acid, which dissolves out nine-tenths of the metal. The high percentage of sulphur (up to 8·65 per cent.) was confirmed. The pigments in the tumour and in the urine are identical. There is a precursor, melanogen; it is this which is usually passed in the urine. It is colourless, but becomes black on exposure to air, or on the addition of nitric acid (Eiselt's reaction) or other oxidising reagents. Hoppe-Seyler attributed this to admixture with indican, which is frequently present in the urine. The urine gives a black precipitate with very dilute ferric chloride, and with dilute sodium nitroprusside and caustic potash a pink coloration, which turns blue on the addition of acids. The latter reaction is not due to melanin, but to some substance excreted simultaneously (v. Jaksch). Brandl and Pfeiffer confirmed Mörner's results, and agree, in opposition to Nencki, that melanin is derived from hæmoglobin. Sheridan Lea's criticism is to the point, and should be borne in mind in considering iron reactions in sections. "Some of the melanins may contain iron, some none, but whether they do or do not is not a decisive test of their derivation. If they do, it makes the connection more probable; if they do not, they may still take their origin from blood-pigments, as in the highly-coloured but iron-free hæmatoporphrin."

Kerschbaumer lays down the following rules for the differential diagnosis of autochthonous and hæmatogenous pigmentation:

(a) In autochthonous pigmentation the pigment-cells are uniformly distributed; in hæmatogenous irregular clumps occur near extravasations or along the vessels.

(b) In autochthonous pigmentation there is brownish-black coloration and uniform fine granulation; in hæmatogenous the colour is golden to deep brown, and there is irregular coarse granulation.

(c) In autochthonous pigmentation the cells resemble normal chromatophores; in hæmatogenous they differ greatly in size and shape.

(d) In autochthonous pigmentation no iron reaction is given; in hæmatogenous this is present, especially in the stage of coarse granulation. (It must be noted that the iron reaction fails in the earliest and latest stages of hæmatogenous pigmentation.)

The following are the best tests for iron in sections:

(1) *Perls' reaction*.—Place sections in 2 per cent. ferrocyanide of potassium for a few minutes, then in $\frac{1}{2}$ –1 per cent. hydrochloric acid. Longer treatment is sometimes necessary, especially after hardening in Müller's solution. Iron-containing pigment stains blue.

(2) *Quincke's reaction*.—Place sections in sulphide of ammonium for 5–20 minutes. The iron appears in the form of dark green or black granules. In the latter case it cannot be distinguished from other pigment.

(3) *Hall's reaction*.—Fresh specimens are placed in a mixture of sulphide of ammonium and alcohol for twenty-four hours, then hardened in alcohol. Sections are treated with ammonium sulphide or a mixture of 1·5 per cent. potassium ferrocyanide and 0·5 per cent. pure hydrochloric acid for twenty minutes. Quincke's or Perls' reaction is then more accurately obtained.

(4) *Macallum's reaction*.—Place sections in sulphuric acid alcohol in an incubator at 35° C. for twenty-four hours. Wash in alcohol, and stain with 0·5 per cent. solution of pure hæmatoxylin in distilled water.

Granular pigment giving the iron reaction was called hæmosiderin by Neumann; it is an albuminate of iron derived from hæmoglobin. Its relationship to melanin has been examined by Abel. Langhans observed that the coarse granules gradually break up into fine ones, which later dissolve, become diffuse throughout the protoplasm, and are finally absorbed. Various authors have observed the absence of iron reaction in hæmatogenous pigment (Perls, Kühlenkamp, Oppenheimer, Decking, etc.). That a causal relationship exists between pigment formation and the development of blood-vessels has been shown by various embryologists (Kessler, Kölliker, Ehrmann). Hæmatogenous pigmentation frequently occurs in conjunction with autochthonous. According to Kerschbaumer the cells of the growth act as phagocytes and take up blood-corpuscles which have passed through the vessel walls by diapedesis or have been extravasated; she has observed all stages of degeneration within the cells. Blood-pigment may occur in the nuclei of the vessel walls and within the lumina (Leber, Ziegler, Schieck). Even the retinal pigment epithelial cells may take up blood corpuscles (Leber). Non-pigmented cells may also become pigmented in a melanotic growth, *e. g.* endothelium (Fuchs); a good example is the

not infrequent pigmentation of epithelium over a melanotic sarcoma. Lagrange gives good figures of hæmatogenous pigmentation.

GINSBERG.—Grundriss der path. Hist. des Auges, Berlin, 1903. RIEKE.—A. f. O., xxxvii, 1, 1891. RIBBERT.—Ziegler's Beiträge, xxi, 1897. E. v. HIPPEL.—A. f. O., xl, 1 and 4, 1894. LEBER.—A. f. O., xlv, 3, 1897. SCHWALBE.—C. f. allg. Path., xii, 1901. TASHIRO.—A. f. O., liv, 2, 1902. VIRCHOW.—*Loc. cit.*, 1863. V. RECKLINGHAUSEN.—Lehrbuch. WALDEYER.—Virchow's Archiv, xli. MERTSCHING.—Virchow's Archiv, cxvi. RITTER.—A. f. O., xi, 1, 1865. ZIEGLER.—Lehrbuch, 1892. LANGHANS.—Virchow's Archiv, xlix, 1870. GUSSENBAUER.—Virchow's Archiv, lxiii, 1875. VOSSIUS.—A. f. O., xxix, 4, 1883; xxxi, 2, 1885. BIRNBACHER.—C. f. A., viii, 1884. OPPENHEIMER.—Virchow's Archiv, cvi, 1886. VIRCHOW.—Virchow's Archiv, i. BERDEZ AND NENCKI.—Arch. f. exp. Path., xx, 1886. MÖRNER.—Z. f. phys. Chem., xi, 1887; xii, 1888. V. JAKSCH.—Z. f. phys. Chem. xiii, 1889. BRANDL AND PFEIFFER.—Z. f. Biol., xxvi, 1890. SHERIDAN LEA.—In Foster, Text-book of Physiology, Appendix, London, 1892. NEUMANN.—Virchow's Archiv, iii, 1888. ABEL.—Virchow's Archiv, cxx. PERLS.—Virchow's Archiv, xxxix, 1867. QUINCKE.—Arch. f. exp. Path., xxxvii; Arch. f. klin. Med., xxvii. MACALLUM.—Jl. of Phys., xxii, Suppl. KÜHLENKAMPF.—Inaug. Dissert., Würzburg, 1866. DECKING.—Inaug. Dissert., Würzburg, 1887. KESSLER.—Zur Entwicklungsgeschichte des Auges der Wirbelthiere, Leipzig, 1877. KÖLLIKER.—Verhandl. d. physik.-med. Gesellsch. zu Würzburg, xvii, 1883. EHLMANN.—Bibliotheca Med., 1896.

Degeneration.—Degenerative changes in the cells are the rule in the more extensive sarcomata of the uveal tract, they are least evident in the spindle-celled type, and most so in the angiosarcomata.

The most frequent change is *hyaline degeneration*. It attacks especially the vessel walls, which become thickened and homogeneous, staining conspicuously red with eosin and van Gieson. The nuclei become sparse, and the hyaline change may attack the inner side of the wall, leading to partial or complete obliteration of the lumen, the endothelium disappearing. The fibrous stroma is also affected, so that patches of degeneration occur. The cells swell, become spherical and homogeneous, the nuclei undergoing the same changes and losing their affinity for dyes. They may become transformed into round or irregular masses. These changes often occur in the round-celled type. Kerschbaumer occasionally obtained an *amyloid* reaction.

Glycogen has been observed by Panas, Best, and Kerschbaumer. It appears as globules and sickle-shaped deposits in hardened specimens. It is best seen in fresh preparations, but also after hardening in absolute alcohol (Best). It is soluble in saliva; it stains brown with Lugol's iodine solution, and is then soluble in water and more so in glycerine. It often stains by Weigert's method: this also attacks the pigment (Birnbacher). It does not stain with iodine and sulphuric acid, methyl violet, or acid fuchsin; it stains with carbol fuchsin. Best gives the following directions for staining: (1) Stain with strong solution of iodine in potassium iodide and 50 per cent. alcohol; wash out in iodised absolute alcohol; origanum oil, balsam; (2) stain 15–30 min. in carbol fuchsin, wash rapidly in $\frac{1}{2}$ per cent. hydrochloric acid alcohol, decolorise quickly in absolute alcohol. The sections may be previously counterstained with hæmatoxylin.

Myxomatous degeneration also occurs, especially in angiosarcomata. It attacks the vessel walls (Kerschbaumer), and also the fibrous stroma between the tubules of cells (Coppez). Large areas may be affected. It is a true myxomatous degeneration, as shown by the

presence of mucin, which stains differentially with thionin, toluidin blue, mucicarmin, and muchæmatin.

Fatty degeneration is shown by the appearance of fat globules in the cytoplasm, which soon becomes filled, so that the nucleus is invisible. The cell finally breaks up, setting free the fat.

Necrosis is shown by areas in which the nuclei fail to stain. Extensive necrosis may occur as the result of hæmorrhages. The degenerated material may become absorbed, with the formation of cystic spaces of various sizes, which may contain fat, cholesterin, pigment, etc. The necrosis in ordinary choroidal sarcomata is always patchy and relatively localised. There is a type in which practically the whole tumour is necrotic. These cases would probably have gone on to phthisis bulbi if the eyes had not been excised (*v. infra*).

Calcareous deposits in the degenerated areas are said to occur, but are rare.

PANAS.—A. d'O., xvi, 1895. BEST.—Ziegler's Beiträge, xxiii, 1898; B. d. o. G., 1901. COPPEZ.—A. d'O., xxi, 1901.

Hæmorrhage.—Small hæmorrhages are common in choroidal as in other sarcomata. Verhoeff found comparatively large hæmorrhages in 25 out of 55 cases examined. I have also noticed them not infrequently. Verhoeff records 3 cases with very extensive hæmorrhage, and points out the danger of overlooking such cases and mistaking them for hæmorrhagic glaucoma, etc. In 21 of Verhoeff's cases necrosis of the tumour was a marked feature, and is regarded as the commonest cause of hæmorrhage. The necrosis in turn is probably most often due to anæmia, resulting either from a degenerated condition of the vessels or from compression of the latter by the tumour. On the other hand, necrosis as a result of the extravasation must not be overlooked. In rare cases hæmorrhage takes place from the atrophied choroid, iris, or ciliary body. Possibly some cases of choroidal sarcoma with phthisis bulbi are due to organisation of a blood-clot in the vitreous chamber (Verhoeff). Hæmorrhage may be the cause of sudden onset of glaucoma. A case with recurrent hæmorrhages has been described by E. v. Hippel.

VERHOEFF.—A. of O., xxxiii, 1904. E. v. HIPPEL.—A. f. O., xl, 4, 1894.

Histogenesis.—Primary sarcomata of the choroid might conceivably arise from either of the layers of the choroid or from any of the fixed cells found within it.

All the layers of the choroid are pigmented with the exception of the choriocapillaris. It was therefore a reasonable suggestion that melanotic sarcomata originate in the external layers, whilst leucosarcomata spring from the choriocapillaris. Brière (1873) first stated the proposition in these definite terms, although Knapp (1868) had earlier called attention to the choriocapillaris as a suitable nidus for sarcoma, which might, then, be expected to show great vascularity, loose texture, and relative freedom from pigment. Fuchs (1882), in his monograph, opposed the theory, stating that all sarcomata of the choroid originate in the deeper layers. Schieck (1898), basing his results upon 10 cases,

concludes that white tumour areas connected with the surface of choroidal sarcomata, having remnants of choriocapillaris in their structure, and showing a characteristic angiosarcomatous or endotheliomatous structure, in all probability spring primarily from the choriocapillaris. Proliferation of the deeper layers is in these cases secondary, and the invasion of these layers is no proof of the origin of the growth from them. In the later stages any primary leucosarcoma of the choriocapillaris may become pigmented, owing to invasion of the pigmented layers leading to erosion of vessels and proliferation of chromatophores, as well as transference by embolism. That remnants of the choriocapillaris should be found on the surface of these tumours is not surprising, and the balance of evidence is against Schieck's view.

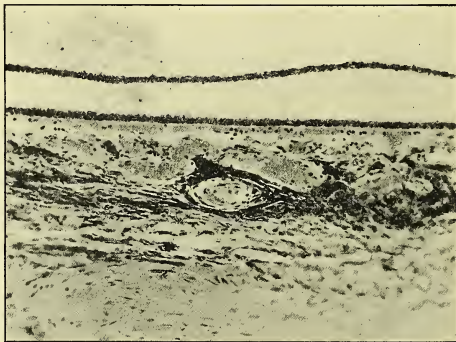


FIG. 376.—SARCOMA OF THE CHOROID. $\times 120$.

From a specimen sent by Professor Fuchs. Very early stage of sarcoma of the choroid, showing proliferation of chromatophores. (See B. d. o. G., 1900.)

It cannot be definitely disproved until the earliest stages of leucosarcomatous proliferation are observed (*cf.* Wintersteiner, *v.* p. 519).

Most sarcomata of the choroid undoubtedly spring from Haller's layer (Fuchs), some probably from Sattler's layer and possibly the suprachoroidea. The suprachoroidea was unaffected in all of Kerschbaumer's cases.

With regard to the cellular origin of the tumours the chromatophores and the endothelium come most under discussion. The normal structures are so quickly disorganised that it is extremely difficult to settle the question in individual cases. No deductions can be drawn from the conditions at the edge of the tumour, which represents, not an area of origin, but merely an area of extension (Ginsberg). The sarcoma cells here are not necessarily derived from the preformed elements, but from the invading cells. In the case of melanotic tumours there can be no doubt that the pigmented cells arise from the

chromatophores. The occurrence of pigmented "nævi," or groups of densely packed and deeply pigmented chromatophores, is of interest in this connection. Such a case has been described by Purtscher. Very interesting too is the case described by Fuchs as a commencing sarcoma (Fig. 376). In the neighbourhood of the macula there were groups of thickly packed, short, brown pigmented spindle cells, arranged chiefly along the arteries in Haller's layer. The cells were not cells of the adventitia, but branched pigment cells and non-pigmented endothelial cells, such as occur in the suprachoroidea and intervacular spaces. The branched pigment cells became shorter and thicker. The non-pigmented endothelial cells showed on each side of the flat nucleus more and more protoplasm, at first non-pigmented, and later containing more and more pigment granules. The cells thus became thicker, until they were finally short pigmented spindle cells like the branched ones. In the discussion upon this case Wintersteiner stated that he had twice by chance lighted upon commencing sarcomata of the choroid. One was a leucosarcoma, the other melanotic; in each case the tumour lay in Haller's layer.

As already mentioned, Ribbert thinks that the non-pigment cells are also derived from the chromatophores, even when they look like endothelial cells and are arranged in quasi-alveoli. These are round and non-pigmented simply because they are young. The larger, deeply pigmented round cells are, according to this author, contracted chromatophores. Fuchs so far agrees with this view in saying that the more pigment is developed the rounder the cells become. Ribbert and Tashiro also consider the ingrown retinal epithelial cells as merely contracted chromatophores. This seems to be negated by the fact that they can take up blood-pigment and give the iron reaction, whereas chromatophores do not (E. v. Hippel, Leber). Tashiro thinks that several chromatophores can unite, forming one large cell. Ribbert suggests the term *chromatophoroma* for the growths, or in default of that, melanoma. The former is cumbrous, and rests on an unproved theory; the latter adds to the confusion which already exists in the use of this word.

Fuchs in his monograph (1882) expresses the opinion that the non-pigmented adventitia cells of the deeper layers first proliferate in sarcoma formation. These stimulate proliferation in all the neighbouring cells, including the chromatophores. If we lay more stress on the proliferation of the perivascular endothelial cells, this view is still the most probable. It is not likely that the pseudo-alveolar types of sarcoma arise from proliferation of the chromatophores. There are three fairly definite types of the alveolar growths, viz. the tubular type, in which the blood-vessels have a thick mantle of stratified cells (Knapp, Günther); the type in which the "alveoli" are bounded by blood-vessels, which form a network the meshes of which contain the cells (van Duyse); and the type which most nearly approximates the true alveolar, in which the lymph spaces are distended with cells (Coppez). In all of these an endothelial origin is the simplest hypothesis, but it is too doubtful to authorise calling these tumours definite endotheliomata.

In considering the possible endothelial origin of many sarcomata of

the choroid, the normal distribution of endothelium must be borne in mind (v. p. 442). It will be noticed that the choroid does not contain lymph vessels or tubules, but only lymph spaces or clefts. This endothelium is, therefore, interfascicular, and has no intimate relationship with the vessels. Besides this there is the endothelium of the perivascular lymph spaces, which is indissolubly bound up with the vessels. Hence Coppez, who has specially studied the question, considers that there are two types of endothelioma, the *interfascicular endothelioma* and the *perithelioma*. Now, various factors which occasion confusion must be taken into account. In endotheliomata in other parts of the body it is unusual for one type of endothelium to take an abnormal growth without other types being also affected. It is only in the earliest stages, and occasionally at the advancing edges of the tumour, that the proliferating elements can be made out. Secondly, distortion of the normal tissues rapidly occurs. Thirdly, others seem to be infected by the abnormal processes which are going on, and they in turn take on an abnormal type of proliferation. Fourthly, none of these abnormally proliferating elements reproduce their respective types accurately; they tend to approximate either embryonic types or even diverse types, even if actual transition from one type to another does not actually occur (metaplasia, v. Hansemann). Hence endotheliomata may nearly resemble carcinomata and have frequently been mistaken for them (for a good example see Knapp).¹ In the choroid the reverse may occur, a metastatic carcinoma being diagnosed as endothelioma (e.g. v. Krüdener). The endothelial cells, too, may become spindle-shaped or asteroid, so that many are diagnosed as other types of sarcoma (see probable examples in Coppez). Fifthly, degenerative changes occur, masking the mode of development, and indeed endotheliomata are especially prone to hyaline, mucoid, and cystic degeneration.

All these and many other factors obscure the histogenesis of individual tumours, quite apart from the difficulty of distinguishing the endothelial cells themselves. The earliest change observed in these is swelling of the nuclei, so that the characteristic nucleoli stand out more prominently; the cytoplasm also swells and becomes fusiform. The cells rapidly proliferate and are arranged in series in the lymph-space. By mutual pressure they become polygonal, except such as are terminal. The nuclei stain more faintly with hæmatoxylin than the surrounding cells, and the cytoplasm more deeply with eosin. It is always open to look upon the endothelial proliferation as a mere reaction of these cells to the stimulation of true malignant growth in the neighbourhood.

It is noteworthy that the typical networks of bands of endothelium which occur in undoubted endotheliomata elsewhere—in the skin and salivary glands (Volkmann),² kidney (Manasse),³ etc.—never occur in the choroid. The absence of true lymph-vessels may be adduced as a possible explanation. The nearest approach to the typical structure is perhaps found in Lagrange's "lymphangiosarcoma" (v. p. 509).

The endothelium within the vessels is another available source of

¹ KNAPP, A. f. A., iv, 1875.

² VOLKMANN, Z. f. Chir., xli, 1895.

³ MANASSE, Virchow's Archiv, cxliii, 1896.

endothelioma; such a case is described by v. Krüdener, but it was probably a metastatic carcinoma. Proliferation in this situation, so common in inflammatory and degenerative conditions, is conspicuously rare in malignant growths.

No deductions can be drawn from the character of extra-bulbar extensions and metastases as to the histogenesis of the primary growth. In the orbital tissues a pseudo-alveolar arrangement is not uncommon, and is simply dominated by the environment. This, too, often reacts upon the cells, causing marked alterations in their character. Relief from the intra-ocular tension leads to more exuberant growth. Fine vessels are often seen here filled with cells.

Even the tubular angiosarcomata are not necessarily true peritheliomata. This is shown by Ribbert's observation of the manner in which chromatophores cling to the vessels and proliferate in layers around them, and also by Fuchs's early sarcoma (Fig. 376). The typical arrangement in glioma is an unexceptionable analogy (Ginsberg).

Sarcomata of the choroid are not infrequent in which different parts show very diverse structure. Sharply limited areas of pigmentation are sometimes a striking feature. Alveolation may be present in portions of the growth and absent in others (Schieck). Chromatophores are almost invariably found even in angiosarcomata. It is well nigh impossible that these are all remnants of the normal structures, or that they have wandered in, or been carried in, as emboli (Schieck). One is led irresistibly to the conclusion that proliferation of various types of cells takes place as a fundamental characteristic.

BRIÈRE.—Thèse de Paris, 1873. SCHIECK.—A. f. O., xlv, 2, 1898; xlviii, 2, 1899. GINSBERG.—Grundriss, 1903. PURTSCHER.—A. f. O., l, 1900. FUCHS, WINTERSTEINER.—B. d. o. G., 1900. VAN DUYSSE.—A. d'O., xvi, 1896. GRIFFITH.—T. O. S., xix, 1899. *COPPEZ.—A. d'O., xxi, 1901. v. KRÜDENER.—A. f. A., xxxi, 1895.

Changes in other parts of the eye.—The choroid is usually unrecognisable at the part covered by the tumour; remnants may be found—apart from the blood-vessels—in the form of elastic fibres which have escaped destruction, and are made evident by specific stains. Remnants of the suprachoroidea are generally present, and this may be intact. On the other hand, it may be entirely destroyed, the tumour being seated directly upon the sclerotic. The superficial and middle layers of the choroid can generally be traced a considerable distance on to the inner surface of the growth. If the latter is lens-shaped or round, Bruch's membrane is intact; if it is mushroom-shaped, the lamina vitrea will be found ruptured, the wavy ends being situated at the neck of the tumour. There is often new-formed fibrous tissue on the surface of the growth, and this may extend some distance beneath Bruch's membrane, replacing the choriocapillaris: it often contains hæmatogenous pigment. It may become ossified so that the sarcoma has a bony shell (Leber).

At the edges the tumour generally slopes gradually if it is small and lens-shaped, more abruptly if larger and more rounded. There is often round-celled infiltration here. The cells may be in part young sarcoma cells, though they are probably for the most part evidence of inflammatory reaction. The blood-vessels of the choroid are often compressed,

so that there is congestion on one side and anæmia on the other. This is particularly marked when the tumour is situated between the disc and the equator. Here the arterial and venous streams are both in the same direction—forwards, so that the vessels are widely dilated behind the growth, and empty in front of it (Knapp). There are often hæmorrhages in the choroid as the result of the pressure.

The retina over the growth may be *in situ* if the tumour is small. I have seen it under these circumstances separated by a thin layer of red corpuscles; before excision there was only a relative scotoma for colours. More frequently the retina is detached, often over a wider area than the growth occupies. Over mushroom-shaped growths it often touches the summit, and slopes off at the sides, the space being filled with albuminous fluid, which coagulates on hardening, and contains leucocytes, pigment cells, free pigment granules, etc. The retina then shows degenerative changes, which vary in degree according to the length of time which has elapsed since detachment. It may be bound down in places to the fibrous tissue on the tumour. I have observed in several cases early simple detachment in the lower hemisphere as well as that caused by the growth (*cf.* Fig. 261, Vol. I); in the case referred to above there was an absolute scotoma over this area. This simple detachment is probably due to fluid being poured out from the irritated choroid; the fluid gravitates to the lowest part and causes detachment of the retina there (Parsons). Bruns describes invasion of the retina at an early stage, with splitting of the layers; this must be a very rare occurrence. When the tumour is large complete detachment occurs, the usual umbrella shape being modified by the pressure of the neoplasm. Still later the retina shrinks together into folds, stretching behind the lens over the growth to the optic disc. It then shows more marked degeneration, amounting to atrophy where pressure is greatest. It finally becomes disorganised and invaded by the tumour-cells, so that only fragments are recognisable in places. The pigment epithelium always shows changes. It remains attached to the tumour for the most part, and parts may grow into it or be surrounded by it; this only occurs after rupture of Bruch's membrane. The pigment epithelium may be raised by isolated nodules of cells; these are regarded as local metastases by Leber and Bruns. Some pigment cells are cast off into the subretinal space. Some cells proliferate, others degenerate, becoming vacuolated and losing their pigment; others, again, fuse into clumps. In the very necrotic type of peritheliomata (*v. infra*) the retina and other parts of the eye are also almost entirely necrosed. Here the retinal capillaries may sometimes be seen to have undergone hyaline degeneration, followed by deposition of calcareous salts (Fig. 377).

Changes in other parts of the eye are usually minimal as long as the tumour is small. The only important exception is the occasional presence of pigmented cells in the angle of the anterior chamber. These have been studied especially by Panas and Rochon-Duvigneaud, Niesmanoff, and E. v. Hippel. They are not sarcoma cells, but leucocytes which have taken up pigment granules, have been carried away by the lymph-stream, and caught in the meshes of the ligamentum pectinatum. They never lead to metastatic deposits here, though

they doubtless impede the exit of lymph and help to cause rise of tension.

Eyes containing melanotic sarcomata have been found occasionally to be very deeply pigmented in other parts. Treacher Collins has recorded such a case, in which a melanotic sarcoma of the ciliary body was associated with deep pigmentation of the whole uveal tract and pigment patches in the sclerotic; the other eye showed no abnormal pigmentation. Cases of progressive pigmentation of the conjunctiva, etc., occur (*v.* Vol. I, p. 110), and the question arises whether this is evidence of predisposition to sarcomatous development. There is some reason to think that it is, though such cases are extremely rare:



FIG. 377.—CALCIFICATION OF RETINAL CAPILLARIES. $\times 100$.
From the same specimen as Figs. 378-381. Parsons, T. O. S., xxv.

melanosis of the sclerotic is not especially associated with sarcoma, except, of course, in those cases due to extra-bulbar extension.

We have already seen that secondary glaucoma is the typical outcome of continued development of the tumour. This is due to encroachment upon the intra-ocular space, whereby the retina and vitreous are pressed upon, the pressure being transmitted to the lens, which is forced forwards, so that the periphery of the iris is brought in contact with the back of the cornea. The filtration angle thus becomes blocked, and the intra-ocular tension rises. That this mechanism alone suffices is seen in the rarer cases of sarcoma at the posterior pole, in which glaucoma supervenes before detachment of the retina. It is certainly aided by cellular blockage of the spaces of Fontana, and in many cases by pressure upon the *venæ vorticosæ*. In the vast majority of cases retinal detachment precedes increased tension, and the latter is largely due to this factor. This is proved by the fact that there is no

definite relationship between rise of tension and size of growth—glaucoma may come on early with small tumours and be absent with large ones, though this is often due to the nature and extent of vascular obstruction. Diffuse sarcomata, for example, usually lead to early glaucoma, slowly growing spindle-celled sarcomata to late onset of tension (Kerschbaumer).

Secondary glaucoma rapidly passes into the congestive type, with extreme congestion of the anterior ciliary vessels—often showing localising signs in accordance with the site of the tumour, and severe iritis. All the anatomical signs of glaucoma, including cupping of the disc, staphylomata, etc., supervene, and require no special consideration here.

More interesting is the smaller yet still considerable group of cases in which iridocyclitis is a marked feature. It replaces the usual glaucomatous stage, and manifests all the symptoms and anatomical signs of the simple inflammatory disease, and like it, goes on to shrinking of the globe. There is, indeed, evidence to show that it may cause sympathetic ophthalmia (Pagenstecher, Lawrence, Schüppel, Knapp, Hirschberg, Knies, Angelucci, Noyes, Brailey, Milles, Lawford, Leber, Pawel; *see* also Schirmer)—and that, too, independently of any operation on the eye. The occurrence of iridocyclitis was early recognised, and is discussed by Fuchs (1882). Attention was drawn to it again by Ewetzky (1896), and almost simultaneously and more exhaustively by Leber and Krahnstöver (1897-8). v. Graefe (1868) considered that phthisis bulbi in these cases was due to suppurative keratitis, leading to panophthalmitis. This, however, rarely takes place; it is chiefly dependent upon extensive degenerative and necrotic processes. Ewetzky considers the inflammation due to the irritating effects of the products of degeneration; Leber and Krahnstöver, on the other hand, are inclined to refer it to infection, the necrotic parts offering a suitable nidus for pathogenic organisms.

Leber and Krahnstöver collected 34 cases in which phthisis bulbi supervened upon sarcoma of the choroid, 22 cases in which there was more or less reason to suppose that the phthisis bulbi preceded the development of the sarcoma, and 34 cases in which injury might be considered to be the cause of choroidal sarcoma. Analysis of the cases tends to show that the first group is much better authenticated than the second. There is a feeling current that sarcoma is more likely to grow in a shrunken eye than in a normal one. It probably originated in the opinion expressed upon the subject to that effect by Virchow; it is not borne out by careful investigation of the statistics. Similarly there is little to support the view that traumatism is an ætiological factor. Those specially interested in these topics cannot do better than consult this very philosophical monograph. Since its appearance other cases of sarcoma of the choroid associated with phthisis bulbi have been published by Ewetzky, 3 cases, Kerschbaumer 3, Pawel 4, Schultz 1, Silex 1, Key 1, Meyerhof 1, Schottelius 1, Bielsky 1, Harms 1, Kipp 1, Reis 1. It is important that every case of the kind should be carefully investigated and published.

The inflammation, which in these cases leads to phthisis bulbi, is

almost always plastic; hypopyon or other purulent products are rare. Occasionally the inflammation is more confined to the posterior part of the globe, and the iris is little affected; such cases may be easily overlooked. There is sometimes diminished tension without actual shrinking (Lawrence, Hirschberg, Lawford and Collins, etc.—10 cases in all; the first two had sympathetic). Other cases with very prolonged sarcomatous development, fibrous tissue, and bone formation did not shrink (Mackenzie, Knapp, Whiting, E. v. Hippel).

I have demonstrated a series of six cases, five of which showed almost universal necrosis, not only of the tumours but also of other parts of the eye—iris, retina, etc. These cases are the preliminary

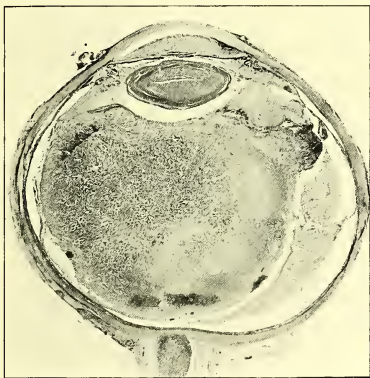


FIG. 378.—SARCOMA OF THE CHOROID. $\times 3$.

Very necrotic sarcoma of the choroid from a man æt. 60. (See Parsons, T. O. S., xxv.)

stage to that of shrinkage of the eye associated with sarcoma of the choroid.

Case 1 was an ordinary melanotic sarcoma of the choroid in the third stage, the extra-ocular extension being unpigmented; the patient died a year after removal of the eye, and was found to have secondary, bile-stained, spindle-celled sarcoma of the liver, and squamous-celled carcinoma of the ribs, lung, and mediastinal glands (*v. p.* 497). Cases 2 (Figs. 378–381) and 3 were almost identical in appearance and general character. They contained very necrotic, round, angiosarcomata of the choroid. There was extensive necrosis of most other structures in the eye. Case 4 had an extraordinary family and personal history: the mother and a younger sister had each had an eye removed at Moorfields Eye Hospital for sarcoma of the choroid, and the patient had had her breast removed for a tumour (*v. p.* 496). There were two small melanotic sarcomata of

the ciliary body and anterior part of the choroid, and a large bilobed, necrotic, angiosarcomatous mass springing from the choroid posteriorly. The other structures of the eye were necrotic, and there were many hæmorrhages. Cases 5 and 6 were necrotic angiosarcomata springing from the choroid at the posterior pole of the eye. The other structures of the eye were also necrotic. A case almost identical with Cases 2 and 3 has been reported by Treacher Collins.

The points specially insisted upon with regard to these cases are: the similarity of the growths macroscopically to organising blood-clots and their apparent origin in the retina—an appearance which was demonstrated to be erroneous (Figs. 378, 379); the varying occurrence of hæmorrhage, the importance of not overlooking sarcoma of the choroid in cases of severe intra-ocular hæmorrhage (*cf.* Verhoeff), and the relation

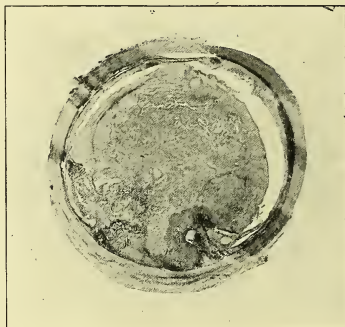


FIG. 379.—SARCOMA OF THE CHOROID. $\times 4$.

From the same specimen, showing the origin of the growth from the choroid.

of the hæmorrhage to the necrosis, whether a cause or a result, both probably occurring; the necrosis, its dissimilarity from the patches of necrosis in ordinary sarcomata, its universality, not only throughout the tumours (Fig. 381), but also in other parts of the eye (Fig. 377). The deductions are, that the necrosis is not due to a preliminary iridocyclitis (*cf.* Leber and Krahnstöver), for there is little inflammatory reaction (infiltration, etc.) inside the eye; that it is not due to thrombosis, and only partially to hæmorrhage, for the intra-ocular tumours are necrosed as a whole, and anastomosis is too free in the eye to permit of this result; that it is probably due to endogenous microbic infection, essentially by means of toxins universally distributed throughout the eye by the intra-ocular fluids, hence the comparative absence of leucocytes. Microbes are also probably present, finding a suitable nidus in the necrotic tissues, hence the slight amount of inflammatory reaction in the less severe cases. The theory is comparable with the

most probable theory of sympathetic ophthalmia, viz. generalised endogenous infection by ultra-visible organisms (*cf.* Römer).¹ It

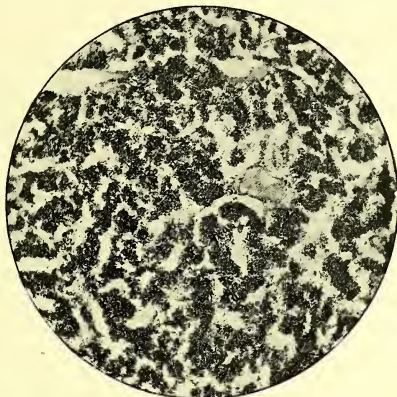


FIG. 380.—SARCOMA OF THE CHOROID. $\times 60$.
From the same specimen, showing structure of the least necrotic part.



FIG. 381.—SARCOMA OF THE CHOROID. $\times 60$.
From the same specimen, showing structure of moderately necrotic part.

explains the marked inflammatory reaction sometimes seen outside the

¹ RÖMER, A. f. O., lv, 2; lvi, 3, 1903.

eye. The growths are probably of relatively low malignancy on account of their genesis (peritheliomata), their necrotic condition, and the thrombosis of the vessels. If, therefore, they were not excised, they would shrink and become examples of shrunken globes containing choroidal sarcomata. Further, they are an early stage of this small group, a stage which has not before been described. That the eyes would inevitably shrink is shown by the albuminous constitution of the intra-ocular fluids, which would lead to diminished filtration and stasis; moreover, the universal necrosis must lead to shrinkage. The growths are also identical in type with those previously found in shrunken globes (*cf.* Leber and Krahnstöver).

Such tumours are probably frequently overlooked, owing to their



FIG. 382.—SARCOMA OF THE CHOROID. $\times 55$.

From a man, æt. 60. A very necrotic sarcoma of the choroid, almost identical with that shown in Fig. 378. Showing moderately necrotic part and degeneration of the vessel walls. (*See* Parsons, T. O. S., xxv.)

great resemblance to intra-ocular blood-clots. They are of great importance practically from the point of view of prognosis, and especially theoretically, since they mark a stage, which has previously escaped observation, in the life-history of a definite group of sarcomata.

*PARSONS.—*Ophth. Rev.*, xxiv, 1905. PANAS AND ROCHON-DUVIGNEAUD.—*Loc. cit.* NIESMANOFF.—*A. f. O.*, xlii, 4, 1896. E. V. HIPPEL.—*A. f. O.*, liii, 3, 1901. TREACHER COLLINS.—*T. O. S.*, xiv, 1894. PARSONS.—*Internat. Congress, Lucerne*, 1904. PAGENSTECHER.—*Würz. med. Zeitschr.*, iii, 1862. LAWRENCE.—*Ophth. Rev.*, ii, 1866. SCHÜPPEL.—*Arch. der Heilkunde*, 1868. HIRSCHBERG.—*A. f. O.*, xxii, 4, 1876. KNIES.—*A. f. A.*, vi, 1877. ANGELUCCI.—*K. M. f. A.*, xvi, 1878. NOYES.—*A. f. A.*, ix, 1880. BRAILEY, MILLES.—*R. L. O. H. Rep.*, xi, 1886. LAWFORD.—*R. L. O. H. Rep.*, xi, 1887. EWETZKY.—*Cercle ophth. de Moscou*, 1897; *A. f. O.*, xlv, 3, 1898. *LEBER AND KRAHNSTÖVER.—*A. f. O.*, xlv, 1 and 2, 1898. V. GRAEFE.—*A. f. O.*, xiv, 2, 1868. VIRCHOW.—*Die krankhaften Geschwülste*, ii, 1863. SILEX.—*Z. f. A.*, i, 1899. JARNATOWSKI.—*A. f. A.*, xxxviii, 1899. SCHULTZ.—*A. f. A.*, xlii, 1901. KEY.—*Widmark's*

Mittheil., Stockholm, 1901. MEYERHOF.—K. M. f. A., xxxix, 1901. SCHOTTELIUS.—Dissert., Freiburg, 1903. BIELSKY.—A. f. A., xlvii, 1903. HARMS.—K. M. f. A., xli, 1903. KIPP.—T. Am. O. S., 1901. REIS.—A. f. A., l, 1904. BERL.—B. z. A., xlix. MACKENZIE.—Diseases of the Eye, 1854. WHITING.—A. f. A., xxiv, 1892. E. v. HIPPEL.—A. f. O., xl, 1 and 4, 1894. NETTLESHIP.—T. O. S., xxiv, 1904. VERHOEFF.—A. of O., xxxiii, 1904. TREACHER COLLINS.—T. O. S., xii, 1892. *PARSONS.—T. O. S., xxv, 1905.

Flat sarcoma, or *diffuse*, or *infiltrating sarcoma* of the uveal tract is extremely rare. The distinction between the circumscribed and diffuse forms was made by Fuchs (1882). Mitvalsky (1894) introduced the term "Flächensarcom"; in France this type is known as "sarcome en nappe ou en plaque." Ewetzky (1898) suggested the term *ring sarcoma*, which well describes their distribution when they attack the ciliary body (q.v.) and iris. I have recently (1904) collected all the cases on record—31 in all; as further proof of their rarity, only one flat sarcoma of the choroid has been found in the Moorfields records (Fig. 383); there is one other doubtful case.

Taking the flat and ring sarcomata together, 16 were male patients, 12 female, 3 unknown; 23 were over 30 years of age, 5 under. The right eye was affected in 15, the left in 11; the side was unknown in 5. The most conspicuous feature in the histories is the long duration of the disease, ranging from seven months to ten years. Circumscribed tumours may recur in the flat or ring form.

Early onset of glaucoma is emphasised by Kerschbaumer, and is attributed to interference with the circulation owing to the extent of the growth and to invasion of the perichoroidal space. Taken in conjunction with the prolonged history, the deduction is open to doubt. In ring sarcoma glaucoma is certainly favoured by the extensive infiltration of the angle of the anterior chamber; here again the process is comparatively slow. Fuchs considered that diffuse sarcomata were particularly prone to iridocyclitis, followed by phthisis bulbi. This view was opposed by Ewetzky, and is certainly not borne out by the collected cases. That there is more inflammatory reaction is probably true, and is shown by the rather extensive development of fibrous tissue in and on the affected parts—especially noted by Mitvalsky, Treacher Collins, and Kerschbaumer.

Extra-ocular extension occurs frequently and relatively early; it is often multiple. It is not conspicuously frequent or early in ring sarcomata. Flat sarcomata tend to erode the sclerotic, probably owing to early invasion of the suprachoroidal space, which is not usually invaded early by the circumscribed type.

These growths are all characterised by their diffuse and infiltrating



FIG. 383.—FLAT SARCOMA OF THE CHOROID.
× 1'5.

Note the thickening of the choroid, and the extra-bulbar nodules.

tendency, as opposed to the formation of a definite tumour. In the case of the ring sarcomata the two conditions are often, in fact,

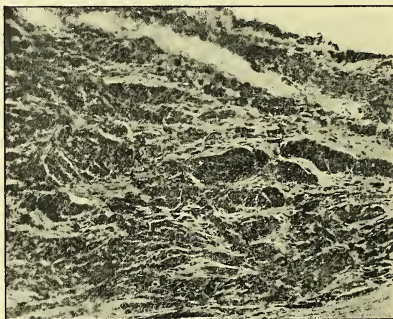


FIG. 384.—FLAT SARCOMA OF THE CHOROID. $\times 60$.

From the same specimen. Showing the alveolar arrangement of a fairly densely pigmented portion of the growth.

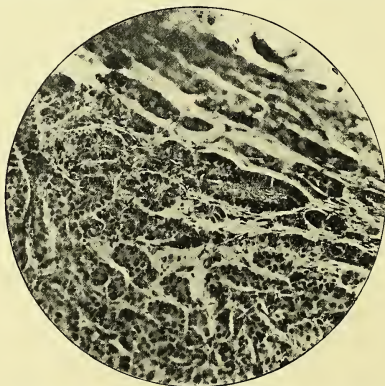


FIG. 385.—FLAT SARCOMA OF THE CHOROID. $\times 120$.

From the same specimen. Showing the alveolar arrangement of a slightly pigmented part near the disc. The cells are distinctly epithelioid.

generally combined: this is never so with the flat sarcomata of the choroid. The cytology of the growths is particularly interesting, and gives some clue to the histogenesis and mode of growth of choroidal

sarcomata in general. The points which particularly impress one in examining the protocols are: (1) the frequency of large round or polygonal cells, often combined with spindle cells; (2) the frequency of an alveolar or plexiform arrangement, either throughout the growths, or in parts, or in secondary extensions (Figs. 384, 385); (3) the frequency of hyaline and myxomatous degeneration, and the occasional presence of necrosis; (4) the frequency of extension along the perivascular lymph spaces surrounding the perforating ciliary vessels and venæ vorticosæ. These characteristics are almost invariable in the flat sarcomata, but are less marked in the ring form. Here there is a preponderance of short thick spindle cells, though oat-shaped and round cells are often combined with epithelioid cells.

The shape and character of the cells have led several authors to diagnose them as endothelial. I am of the opinion that they are almost always, if not always, so, and the growths are endotheliomata. Not only so, but they are endotheliomata as opposed to peritheliomata (*cf.* Coppez). Their endothelial origin is much supported by the three other characteristics mentioned above. An alveolar or plexiform arrangement and great tendency to myxomatous degeneration are features commonly found in endotheliomata. Such an origin too readily explains the ease and rapidity with which they invade all the lymph spaces in the neighbourhood. The growths vary much as regards pigmentation, which must be regarded as an epiphenomenon, and no contra-indication of endothelial origin.

The retina is not usually detached in these cases, probably owing to the flatness of the growths. The view expressed by Fuchs that diffuse sarcomata may ultimately fill the globe was early opposed by Mitvalsky, and is not borne out by subsequent investigations. Secondary nodules are not uncommonly found in the retina: this is explained by their diffusely infiltrating character rather than by the proximity of the undetached retina. Bruch's membrane is usually intact, and extension to the retina takes place at the edge of the disc.

The essential characteristic of these growths—their diffusely infiltrating tendency—remains to be explained. The key to this will, I think, be found in their flatness and in their endothelial origin. I have elsewhere¹ brought forward an explanation for the flatness of metastatic carcinoma of the choroid (*v. infra*) and the prominence of the ordinary circumscribed sarcoma. The ordinary primary sarcoma starts in the actual stroma-cells of the choroid itself. Following the laws of growth, the cells proliferate in the directions of least resistance. Since the growth commences in the actual tissues themselves, the resistance is equal in all directions at first, so that at this stage we might expect the tumour to be spherical. Soon the greater resistance on the side of the sclerotic makes itself felt—the advance is less in this direction whilst equal in other directions; hence the tumour becomes roughly ellipsoidal, growing twice as fast laterally as in thickness. This mode of advance continues until the membrana vitrea is burst through, which results from equable stretching rather than from any localised attack by the growth upon any one spot. At the hole in Bruch's mem-

¹ PARSONS, R. L. O. H. Rep., xv, 3, 1903.

brane, which is necessarily central as to the surface of the tumour, resistance is greatly relieved; proliferation becomes most active in this direction, and a new focus is established in the subretinal space. Here again resistances are equalised, growth proceeds equally in all directions, and the very characteristic globular head of the tumour is formed, connected with the main mass by a short neck at the level of the lamina vitrea.

In metastatic carcinoma the growth is along the lymph-spaces in the choroid. We should expect that a growth originating in the cells lining these lymph-spaces would exhibit similar peculiarities. In both cases the cells lie *between* the planes of the choroidal stroma. We



FIG. 386.—FLAT SARCOMA OF THE CHOROID. $\times 60$.

From the same specimen. Showing a typical spindle-celled portion, near the optic nerve. It may be noted that these parts showed much more definite attempt at tumour formation, being rounded, as if growing equally in all directions.

know from the frequent cases of detachment of the posterior part of the ciliary body that traction readily draws the planes of the stroma of the uveal tract apart, and that those which offer most resistance and persist longest are those which are more or less concentric with the curvature of the globe, those transverse or oblique to this direction being relatively feeble. The same is shown in the further growth of these neoplasms. Lying as the cells now do between these concentric planes, the directions of least resistance are along them; hence most of the growth is lateral, a minimum increase of thickness taking place.

The same explanation applies, I think, to flat sarcomata. In a sense they are tumours *in* the tissue, but not *of* it. They spring from lining cells and proliferate in the spaces which they line, following these spaces in all their ramifications, subject only to the physical

conditions of resistance. The opposing forces are least in the circle of the angle of the anterior chamber, and along this they progress. This, and their slowness of growth, characteristic of most endothelial growths, explains the relative infrequency of epibulbar extension, resistance being usually, but not invariably, greater in that direction. When it does occur it will be along the perivascular lymph spaces of the anterior perforating vessels, and will probably be determined by immediate proximity to these of the original focus.

NETTLESHIP.—*Trans. Path. Soc.*, xxvii, 1876; xxix, 1879. FUCHS.—*Loc. cit.* MITVALSKY.—*A. f. A.*, xxviii, 1894. EWETZKY.—*A. f. O.*, xlii, 1, 1896; xlv, 3, 1898. MARTENS.—*Virchow's Archiv*, cxxxviii, 1894. TREACHER COLLINS.—*Catalogue of the Museum*, R. L. O. H., Series IV, Sub-series E, No. 35. GROENOUW.—*A. f. O.*, xlvii, 2, 1899. HELLEBERG.—*Mitth. aus d. Augenkl. d. karol. med.-chir. Inst.*, Stockholm, 1899. KAMOCKI.—*Z. f. A.*, iii, 1900. MEYERHOF.—*K. M. f. A.*, xxxix, 1901; xl, 1902. KOPETZKY v. RECHTERBERG.—*A. f. O.*, lii, 2, 1901. *PARSONS.—*A. of O.*, xxxiii, 1904. A. KNAPP.—*A. of O.*, xxxiv, 1905.

METASTATIC SARCOMA

There is no well-authenticated case of metastatic sarcoma of the choroid. Cases have been recorded as such by Brömser, Schiess-Gemuseus and Roth, and Pflüger. In all these cases the primary growth is supposed to have been a congenital nævus—on the cheek, over the sternum, and over the parotid respectively. Fuchs rightly points out that in Brömser's case it is doubtful if the primary growth was a sarcoma, whilst Leber supports the diagnosis. In the second case the papilla was affected, together with the choroid in the immediate neighbourhood. In Pflüger's case no microscopical examination was made.

In all cases of sarcoma of the choroid it is impossible to be absolutely certain that the eye is the primary seat of the disease, but the balance of evidence is entirely in favour of this view. Elschmig holds the opposite view.

BRÖMSER.—*Inaug. Dissert.*, Berlin, 1870. FUCHS.—*Das Sarcom des Uvealtractus*, Wien, 1882. LEBER.—*A. f. O.*, xxxi, 4, 1885. SCHIESS-GEMUSEUS AND ROTH.—*A. f. O.*, xxv, 2, 1879. PFLÜGER.—*A. f. A.*, xiv, 1885. ELSCHMIG.—*A. f. A.*, xxii, 1891.

METASTATIC CARCINOMA

Perls in 1872 recorded the first case of metastatic carcinoma of the choroid. In 1897 Devereux Marshall was able to collect 24 cases; in 1903 I was able to bring the total up to 33 cases. A few cases, however, were missed, and several have been published quite recently. In all about 50 cases have been published. A complete bibliography is given at the end of this article. It is probable that the condition is not infrequently overlooked.

Carcinoma of the choroid is necessarily always secondary, there being no epithelium in the choroid from which a primary tumour could spring. The primary growth is generally in the breast (24 out of 31), rarely in the stomach (3 cases), lung (3 cases), intestines, thyroid, liver, trachea. The left eye is more frequently attacked than the right (13 out of 21 cases); this corresponds with the greater frequency of left

cerebral embolism, and is due to the same cause, viz. the more direct pathway by the left carotid, which comes off from the aorta, whereas the right comes off from the innominate. It is obvious that the condition must be embolic, and this is further supported by the frequency with which both eyes are affected (8 cases out of 29). Similarly there may be multiple foci in the same choroid (Schultze), though this is unusual. The choroid is almost invariably attacked in the posterior part, in the course of the posterior ciliary vessels; a case of metastatic carcinoma of the ciliary body and iris alone, reported by Briehn,¹ is apparently unique.

The predilection manifested for the posterior part of the eye, as well as for the temporal side, is also to be accounted for by the distribution of blood-vessels. The short posterior ciliary arteries are more voluminous and more important on the outer side of the optic nerve (Lagrange). Moreover, the macular region of the choroid is most richly supplied with the smallest capillaries (Leber). The rarity of the disease is explained in part by the fact that the ophthalmic artery comes off at right angles from the internal carotid. There is, therefore, a greater tendency for emboli to pass on into the cerebral vessels than towards the eye. Having once entered the ophthalmic artery, the chances of their passing into the short posterior ciliaries are greatest. These come off from the ophthalmic as two relatively large trunks, which each divide into four or five branches. Malignant emboli have, however, been seen in an anterior ciliary artery (Lagrange), and Briehn's case must obviously have been due to this, or to embolism of a long posterior ciliary artery.

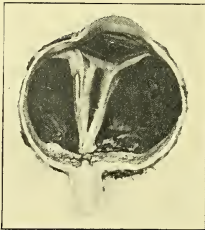


FIG. 387.—METASTATIC CARCINOMA OF THE CHOROID.

Rockliffe and Lister, T. O. S., xxii. The half eye as a mounted specimen, showing the detached retina and infiltration of the choroid with the growth.

The progress of the disease is always very rapid. Vision quickly fails, owing to detachment of the retina, which, at first partial, soon becomes complete. Both eyes may be effected simultaneously, or the second at a short interval after the first—or, of course, it may escape. The tension is seldom raised, probably owing to the short duration of life, for we should expect it to behave in identically the same manner as in flat sarcoma of the choroid. In the cases collected by Marshall tension was normal in 11 eyes, raised in 7, diminished in 4, unknown in 8—30 eyes in 24 cases.

The condition is associated with generalisation of the disease throughout the body. In all the cases which have had a *post-mortem* examination, other organs in addition to the primary seat have been affected. Scarcely an organ seems to have escaped, but the lungs, liver, and meninges are most frequently mentioned. It is not surprising, therefore, that death quickly follows the onset of the condition.

¹ BRIEHN. Dissert., Königsberg, 1902.

The longest period reported is two years (Wagner) ; in the majority of cases it is a few months or weeks. It is obvious that, apart from the relief of pain—which is only rarely present in the eye—no good purpose is served by excision.

There is never a circumscribed tumour, but always a flat thickening of the choroid similar to that met with in flat sarcomata. In exceptional cases parts of the growth are somewhat more prominent (Hirschberg and Birnbacher, Schultze, Uhthoff, Verhoeff). The growth is thickest at the posterior pole, and thins off anteriorly; it rarely reaches the base of the iris (Abelsdorff). In section it is granular in appearance, often with pale spots or networks, which correspond with necrotic areas. The retina is usually detached, being raised only slightly, but over a large area ; this is of some diagnostic importance.

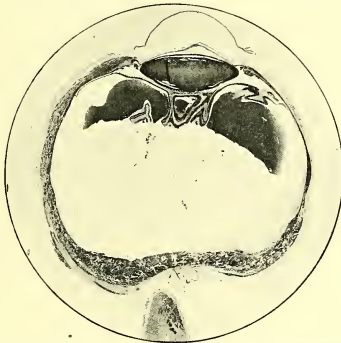


FIG. 388.—METASTATIC CARCINOMA OF THE CHOROID.

From the same specimen. Low power, showing the infiltration of the choroid, and also to a slight extent of the optic nerve. The growth extends forwards on one side as far as the ciliary body.

Histology.—The histology of the growth depends upon the nature of the primary carcinoma, and also varies much independently of this. It is always a glandular carcinoma, with definite alveoli containing epithelial cells, and the differences are those of detail. In none of the cases has there been any difficulty in diagnosis, with the exception of Bock's case, in which an adenoma was diagnosed (*v. infra*). The vast majority of cases are secondary to typical scirrhus of the breast, and the choroidal growth shows evident traces of its origin. It is generally more cellular than the primary tumour, a feature which is not uncommon in secondary carcinomata. Different parts of the growth often vary in this respect.

The more cellular tumours or parts consist of alveoli of various sizes containing large round, or polygonal cells with single large nuclei. There is no intra-cellular stroma, and the stroma between

the alveoli is sparse, consisting merely of the compressed choroidal tissue. The chromatophores are usually degenerated, having lost their processes; the pigment has often escaped, and is aggregated into small clumps. The vessels are flattened out and scarcely visible, though hæmorrhages are frequent both within and outside the affected parts. The tumour rarely consists entirely of this soft medullary type, as was found in Schultze's first case; usually only the more rapidly growing parts have this structure. This is seen when the lamina vitrea is burst through, which only occurs seldom and late. The tumour then grows more quickly and more equally in all directions, so that a round mass is formed. This has never been seen large owing to the lateness of its occurrence.

The true scirrhus type is equally rare, having only been observed



FIG. 389.—METASTATIC CARCINOMA OF THE CHOROID.

From the same specimen. High power, showing the carcinomatous nature of the growth.

by Uhthoff. Here there are great masses of dense fibrous tissue, containing chromatophores and free pigment, rarely in large quantity, with small alveoli, containing comparatively few cells.

Generally the tumour is intermediate in structure between these two types, having parts which are more cellular.

The adenomatous type is seen when the primary tumour springs from tubular glands, as in the stomach, intestines, liver, etc. Such cases have been described by Kamocki, Gayet, Reis, Bock, etc. In Gayet's case there were numerous tubules, lined with cylindrical epithelium. In Kamocki's case the tumour consisted of glandular tissue, in some places resembling the lacrymal gland, in others the thyroid. The epithelial cells were mostly cylindrical, arranged in a single stratum. The peripheral parts had the structure of an acino-tubular gland. The stroma consisted of fibrous tissue containing numerous choroidal pigment-cells. Preparations from the central

portions of the tumour closely resembled a cystoma of the ovary. The cavities were lined with flattened epithelium, and filled with colloid masses containing swollen cancer cells and red and white corpuscles. Papillary processes projected into the lumen. Bock's case presented several peculiarities. There was a definite tumour, deep green in colour, consisting of large polygonal and cylindrical cells arranged in tubules like liver-cells. The lumina of the tubules contained bile, giving the tests for biliverdin. The liver, skin, lungs, muscles, orbit, and arachnoid were all affected. Bock regarded the tumour as an adenoma, but there can be little doubt that Wintersteiner¹ is correct in classifying it with the metastatic carcinomata of the choroid, in this case



FIG. 390.—METASTATIC CARCINOMA.

Rowan, T. O. S., xix. Section of the primary growth in the lung. On the right there is a considerable hæmorrhage.

following a primary liver growth. Reis's case somewhat resembles Kamocki's. The growth was adenomatous in type, with cylindrical cells. These contained vacuoles, and the cyst-like spaces were filled with mucinous material. There were also papillary projections from the walls into the lumen. There was widespread degeneration, so that many of the spaces were filled with amorphous masses.

Degenerative changes.—Degenerative changes are almost invariably found, and are often very marked. The earliest change is probably vacuolation of the cells, such as was present in the case described by me. Here the majority of the cells were vacuolated and many seemed to have disappeared, though they may have dropped out; this is not probable in celloidin sections. A further stage is seen in the develop-

¹ WINTERSTEINER. *Encyklopädie der Augenheilkunde*, Leipzig, 1902.

ment of spaces in the medullary type, such as is described by Schultze, Ginsberg, etc. In Ginsberg's case the growth was secondary to a lung-tumour, and contained spaces and tubules filled with mucus giving the reactions of mucin; the cells showed no degenerative changes, so that it should, perhaps, more properly be regarded as a tubular growth.

Widespread necrosis of the cells is a common feature, large masses of the central cells of the alveoli breaking down into hyaline or granular material, staining red with eosin, yellow with van Gieson. There are occasionally a few leucocytes in and around the degenerated areas. The outer intact cells often stain more deeply than usual with hæmatoxylin. The necrotic area is often excentric, and may reach the edge of the alveoli, communicating with the surrounding stroma, which is also frequently degenerated, and may be represented only by a few

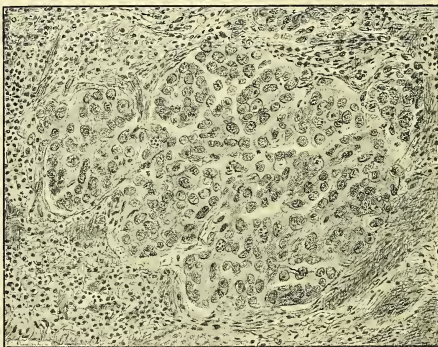


FIG. 391.—METASTATIC CARCINOMA OF THE CHOROID.
Rowan, T. O. S., xix. Section of the growth in the choroid.

chromatophores, which mark out the lines of the original choroidal laminae. Only Uthoff and Ginsberg have described transition stages in the necrotic process, some of the cells showing badly staining nuclei, others diffuse staining. Uthoff found apparently normal blood-vessels in the midst of degenerated masses.

It is not surprising that hæmorrhages are common. The growths commence as malignant emboli, which proliferate and break through the vessel walls. Perls, Uthoff, Mitvalsky, Lagrange, etc., found malignant thrombi in the capillaries. The vessels are also eroded from without, as was seen in the more isolated peripheral alveoli by Abelsdorff. Here the cancer-cells were projecting into the vessels from the side. Elschmig saw evidence of the replacement of the vessels by cancer-cells; he also found two vortex veins obliterated, partly by endothelial proliferation, partly by masses of epithelial cells. Schultze saw a posterior ciliary artery full of cancer-cells as it passed through

the sclerotic. Most of these cases are doubtless due to invasion from without, and it is impossible to be certain that the primary embolus has ever been seen. Hæmorrhage is also induced by the interference with the circulation, which is the principal factor in causing it in other parts of the choroid.

Many authors attribute the necrosis of the cells to hæmorrhage (*e. g.* Mitvalsky, Schultze). Mitvalsky thinks that the necrotic masses are old blood-clots which have become surrounded by the advancing growth. It is more probable that degeneration and necrosis are brought about by malnutrition (Elschnig), many of the vessels being destroyed, and others thrown out of use by thrombosis and compression. The



FIG. 392.—METASTATIC CARCINOMA OF THE CHOROID. $\times 4$.

Parsons, R. L. O. H. Rep., xv. From a woman, æt. 37, four years after removal of right breast for scirrhus.

mere tension under which the cells grow may conduce to dégénération (Lagrange).

The cause of the flatness of the growth of metastatic carcinomata of the choroid is to be sought in the means of propagation along the lymph spaces (*cf.* "Flat Sarcoma"). The tumour starts from a malignant embolus in a capillary or small arteriole. The vessel is blocked, the cancer-cells proliferate and burst through or replace the vessel-walls. They are now situated in the lymph spaces, which lie directly outside the blood-vessels. Hence they lie between the planes of the choroidal stroma. The direction of least resistance is along these planes; hence most of the growth is lateral, a minimum of increase in thickness taking place. The anterior edges of the growth often show an advancing phalanx of cells (Fig. 393), which is particularly striking. Moreover, the mode of growth in the rare cases in which the lamina

vitrea is burst through (*v. p. 536*) tends to support this view, as well as the analogy of the sarcomata.

Changes in other Parts of the Eye.—We have already referred to the frequency of hæmorrhages in other parts of the choroid. These are also usually atrophic, less commonly inflamed and infiltrated; they may contain outlying nodules (Schultze, Holden), which may be either due to multiple primary metastases or to local metastases by the lymph-stream. The supra-choroidea may be intact beneath the tumour, but is generally destroyed. The sclerotic is then usually eroded; it also frequently contains perivascular and interlamellar alveoli. As already mentioned, Bruch's membrane is usually intact, but may be broken through (Ginsberg). In the latter case the tumour



FIG. 393.—METASTATIC CARCINOMA OF THE CHOROID. $\times 60$.

From the same specimen, showing anterior advancing edge of the growth. Note the splitting apart of the choroidal laminae.

proliferates into the subretinal space, forming a globular head, which is never large. Cells frequently get loose in the intra-bulbar space, and are carried by the lymph-stream to other parts of the eye, where they are deposited, and may give rise to local metastases. In this manner tertiary deposits are found in the angle of the anterior chamber (Abelsdorff, *v. Michel*), and even between the ciliary processes (*v. Michel*).

The ciliary body may be involved by continuity or by tertiary, or rarely, secondary (Briehn) deposits. Similarly the iris is also attacked, but whether by continuity alone or by way of the blood or lymph-paths it is impossible to say.

The optic nerve is attacked by way of the lymph-paths. The growth is deposited in the vaginal and perivascular lymph-spaces, and pro-

liferates there, pushing aside and replacing the nerve-fibres. In Uthoff's case the nerve looked of normal thickness, but was found to be entirely replaced by new growth. It may be affected in this manner as far as the chiasma (Schöler and Uthoff, Samelsohn). The nerve is very rarely, if ever, attacked in continuity, the choroidal growth always stopping short at the edge of the disc.

Extra-bulbar growths behind the sclerotic have been observed by Samelsohn, Holden, Schultze, Reis, and others. They show the usual features, but may differ in detail from the intra-ocular tumour; thus Schultze's case had more fibrous tissue in the extra-ocular growth.

The retina has only been involved in the growth in Hirschberg and Birnbacher's case. It is generally separated by fluid, but not always entirely, *e.g.* one of Lagrange's cases.

PERLS.—Virchow's Archiv, lvi, 1872. HIRSCHBERG.—C. f. A., vi, 1882. SCHÖLER AND UTHOFF.—C. f. A., vii, 1883. BOCK.—Virchow's Archiv, xci, 1883. HIRSCHBERG AND BIRNBACHER.—A. f. O., xxx, 4, 1884. MANZ.—A. f. O., xxxi, 4, 1885. SCHAPFRINGER.—Amer. Jl. of Ophth., v, 1888. MITVALSKY (2 cases).—A. f. A., xxi, 1890. GAYET.—A. d'O., xix, 1889. SCHULTZE.—A. f. A., xxi, 1890. EWING.—A. f. O., xxxvi, 1, 1890. GUENDE.—Rec. d'O., 1890. ELSCHNIG.—A. f. A., xxii, 1891. WADSWORTH.—T. Am. O. S., 1890. UTHOFF.—Internat. Beiträge z. wiss. Med., ii, 1891. SAMELSOHN.—Berlin. klin. Woch., 1891. WAGNER.—Ueber metastatischen Aderhauttumoren, Halle, 1891. PORTER.—The Post-Graduate, xvi, 1892. HOLDEN.—A. of O., xxi, 1892. KAMOCKI.—A. f. A., xxvii, 1893. SCHULTZE.—A. f. A., xxvi, 1893. ABELSDORFF.—A. f. A., xxxiii, 1896. NOYES.—T. Am. O. S., 1897. MATTHEWSON.—Brit. Med. Jl., 1897. *MARSHALL (2 cases).—R. L. O. H. Rep., xiv, 3, 1897. KAEMMERER.—Corrbl. des allg. aerzt. Vereins von Thüringen, 1898. DE SCHWEINITZ (2 cases).—T. Am. O. S., 1898. WAGENMANN.—C. f. A., xxii, 1898; and HEDENSTRÖM, Dissert., Jena, 1898 (same case). v. MICHEL.—Inter. Congress, Utrecht, 1899; Beiträge z. Onkologie des Auges, Würzburg, 1899. ROWAN.—T. O. S., xix, 1899. BENTZON.—Hospitals Tidende, ix, 1900. LAGRANGE (2 cases).—Tumeurs de l'Œil, i, Paris, 1901. JACK AND VERHOEFF.—T. Am. O. S., 1902. ROCKLIFFE.—T. O. S., xxii, 1902. BLESSIG.—C. f. A., xxv, 1901. SCHMIDT-RIMPLER.—Lehrbuch, 7th ed., Leipzig, 1901.—HOLDEN.—A. of O., xxi, 1902. *PARSONS.—R. L. O. H. Rep., xv, 3, 1903. GINSBERG (3 cases).—Grundriss, Berlin, 1903. KRUKENBERG.—K. M. f. A., xli, Beilageheft, 1903. REIS.—K. M. f. A., xli, 1903. *OATMAN.—Amer. Jl. of Med. Sc., 1903 (Bibliography). GELPKE.—K. M. f. A., xliii, 1905.

CHAPTER X

THE RETINA

THE NORMAL RETINA

It is outside the scope of this work to enter into an exhaustive description of the minute structure of the retina. (For this, see Schäfer, Greeff, Ramon y Cajal, etc.) In the following brief account only those points of special importance pathologically will be insisted upon.

The retina consists of the following layers from without in: (1) Pigment epithelium; (2) the layer of rods and cones; (3) outer nuclear layer; (4) outer reticular layer; (5) inner nuclear layer; (6) inner reticular layer; (7) ganglion cell layer; (8) nerve-fibre layer.

The *pigment epithelium* consists of low cubical, polygonal—usually hexagonal—cells, with round nuclei. They are smallest and most regular at the posterior pole; in front of the equator they are often large and multinuclear, especially near the ora serrata. They send amoeboid processes between the rods and cones. The pigment granules, which usually mask the nucleus, are short rods, probably crystals, as elsewhere in the retinal pigment cells of the ciliary body and iris. They are thus distinguished from the amorphous granules of stroma pigment, though less so than in many lower vertebrates. The pigment cells have been specially studied by Krückmann.

The *rods and cones* (Schultze) are neuro-epithelial cells, having an outer and an inner segment. They vary in form and distribution in different parts of the retina, cones alone being present at the macula, whilst the rods are most numerous elsewhere. They lie upon a basement membrane, the *external limiting membrane* of the retina, which separates them from the next layer.

Verhoeff, using Mallory's phosphotungstic acid hæmatoxylin, claims to have traced this membrane at the disc into a fenestrated membrane in the pigment epithelium. The epithelial cells project through the holes in the membrane. The whole of this membrane would thus represent morphologically the basement membrane of the central neural canal, the rods and cones being ependymal epithelium.

The *outer nuclear layer* consists essentially of the parts of the neuro-epithelial cells which contain their nuclei. The nuclei of the rods have cross striations and are smaller than those of the cones. The

fibres which pass inwards from these cells are known as *Henle's fibres*. Occasionally isolated cone nuclei lie in or outside of the external

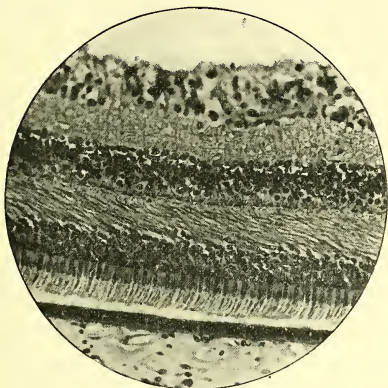


FIG. 394.—NORMAL RETINA.

From a specimen by Verhoeff, stained by Mallory's phosphotungstic acid hæmatoxylin.

limiting membrane, especially in the central parts of the retina (Fig. 395).

These extruded nuclei ("vorgefallene, vorgelagerte Körner") occur



FIG. 395.—EXTRUDED NUCLEI.

Verhoeff, R. L. O. H. Rep., xv. Normal retina, stained by Mallory's phosphotungstic acid hæmatoxylin; showing shortened cones and extruded nuclei opposite a vessel.

most frequently in the posterior part of the retina, around the macula. They are always cone nuclei, and were first described by van Genderen Stort (1887); he thought that they were not a second nucleus to the

cell, but merely the normal one displaced, and this view is correct. Borysiewicz thought that both rod and cone nuclei occurred in this situation. Dimmer found that the cones affected were narrower and shorter than the others. The extruded nuclei seen in normal retinæ are always in small numbers, and lie isolated. Verhoeff considered that they were always opposite a retinal vessel, but this view is incorrect.

The *outer reticular layer* (outer granular or molecular layer [Schultze], outer plexiform layer [Cajal]) or *internuclear layer* (H. Müller) consists of a network of fine nerve-fibres, derived from the bipolars and other cells.

The *inner nuclear layer* contains the rod and cone bipolar cells, with their nuclei. Besides these there are amacrine cells (Cajal), which have no axis cylinder processes, and other cells.

The inner nuclei normally stain more faintly than the outer. In the guinea-pig and frog, with Mallory's phosphotungstic acid hæmatoxylin after formol hardening, only the outer nuclei do not stain (Verhoeff), and this condition is sometimes seen in the human retina, probably always as a pathological phenomenon. Similarly the outer nuclei alone sometimes take on the ordinary hæmatoxylin stain, the inner ones being stained with eosin.

The amount of chromatin, as shown by the Nissl method, is greater in dark adaptation than after exposure to light.

The *inner reticular layer* (inner granular or molecular layer [Schultze], inner plexiform layer [Cajal]) consists of a network of fine nerve-fibrils, chiefly derived from the bipolars. It is much broader than the outer reticular layer.

The *ganglion cell layer* consists of the large multipolar ganglion cells, whose axons form the chief fibres of the optic nerve. They form a single layer except at the macula.

When stained by Nissl's method (methylene blue, thionin, or toluidin blue) the ganglion cells show well-marked Nissl bodies (Bach, Birch-Hirschfeld); these are darkly stained, irregular masses lying in the unstained cytoplasm; they extend into the protoplasmic dendrons, but not into the axon. They vary in size, shape, and arrangement in different animals and at different ages. They also vary according to the adaptation of the eye for light. In dark adaptation the cells are richer in finely granular Nissl bodies, especially at the periphery of the cytoplasm. The chromatin diminishes with exposure to light, and after prolonged exposure to bright light the Nissl bodies break up, vacuoles appear, and the cells shrink. Fibrils in the cells can be demonstrated by a silver reduction method (Bartels).

The *nerve-fibre layer* consists of the non-medullated axons of the ganglion cells as they run towards the disc. It therefore increases in thickness from the periphery towards the papilla, 0·02—0·03 mm. thick 5 mm. from the disc, 0·2 mm. thick 0·5 mm. from the disc on the nasal side (H. Müller). Occasionally patches of medullated fibres are seen near the disc.

The nerve-fibres normally lose their medullary sheaths at the lamina cribrosa medullated fibres in the retina are generally con-

tinuous with the papilla (Fig. 396); rarely they form a patch at some distance from the disc. Opaque nerve-fibres were demonstrated first by Virchow anatomically in the pre-ophthalmoscopic days, and the observation was confirmed by Beckmann, v. Recklinghausen, Schmidt-Rimpler, Manz, and others. Anatomically they usually show varicosities, which are probably artefacts. They were formerly regarded as congenital, but this is not strictly accurate (E. v. Hippel). Medullation occurs from the centre towards the periphery, and is completed last of all cranial nerves in the optic nerve (Westphal). It does not reach the lamina cribrosa before birth, hence the development of medullated fibres in the retina must occur in the early months of post-natal life. It is sometimes associated with other anomalies of the central nervous system—idiocy, etc. (see also "Optic Nerve").



FIG. 396.—MEDULLATED NERVE-FIBRES IN THE RETINA. $\times 12$.
From a specimen by Percy Flemming, stained by Weigert's method.

The nerve-fibre layer is bounded on its inner side by the *internal limiting membrane* of the retina, which lies in contact with the hyaloid membrane of the vitreous.

The whole of the nervous structures of the retina are held together by an epiblastic connective tissue, or neuroglia. The neuroglial cells form thick vertical fibres, *Müller's fibres*, which have wide lateral ramifying processes. The ends of the fibres spread out and interlock with one another, forming the so-called limiting membranes of the retina. The nuclei of these cells are oval, with the long axis vertical, and lie in the inner nuclear layer, and are distinguished from the nuclei of the bipolars by being larger. Other smaller nucleated neuroglial cells occur in the nerve-fibre layer. It has hitherto been found difficult to stain the neuroglial elements of the retina with specific stains (*cf.* Krückmann).

The *macula lutea* is stained yellow by a diffuse colouring matter: the yellow area varies in size, and may be smaller than the fovea (Dimmer). The *fovea* is a depression in the surface of the retina, due to absence of certain layers. The deepest part, 0·12 to 0·3 mm. in diameter, is sometimes termed the *foveola*. There are no rods in the fovea, but the cones are narrow and longer than elsewhere, especially their inner segments. In the foveola the inner segments are again short, and the layers are reduced to the cones with their nucleated fibres, a few cells of the inner nuclear layer, and the pigment epithelium. At the sides the ganglion cells are 6 to 8 deep, and the nerve-fibre layer appears and rapidly increases in thickness. Not only is the *membrana limitans interna* curved outwards, but the *membrana limitans externa* is curved inwards, so that an actual *fovea externa* is produced (Schäfer). The outer nuclear layer of the macula is composed of nuclei only two or three deep, with very long, oblique cone fibres, the outer fibrous layer of Henle being most prominent here. The bipolar cells of the inner nuclear layer are also somewhat obliquely disposed.

At the *ora serrata* the rods and cones first disappear, and then the other layers—all within a zone 0·1 mm. broad. The columnar cells of the *pars ciliaris retinae* are at first somewhat elongated.

The large *blood-vessels* lie in the nerve-fibre layer. The arteries possess an elastic intima lined with endothelium, a media with inner circular and outer longitudinal muscle-fibres, and an adventitia rich in elastic-fibres, the outer ones running longitudinally (Hertel). The media fails first as the vessels diminish in size. The veins are little more than connective-tissue tubes, rich in elastic-tissue fibres, lined with endothelium. Muscle-fibres are very sparse, and only to be found in the large branches (Hertel). The capillaries penetrate to the outer reticular layer, and are therefore absent in the rod and cone and outer nuclear layers, and therefore also in the fovea. They are mere endothelial tubes.

Lymph-vessels are only found as perivascular spaces around the blood-vessels.

Artefacts in the retina.—The retina is almost invariably detached—*i.e.* the inner layers are separated *en masse* from the pigment layer—in eyes embedded in celloidin. Even when frozen and bisected, after hardening in 10 per cent. formol, there is usually a detachment between the disc and the macula (*plica centralis*), and this is often accompanied by a horse-shoe-shaped fold beyond the macula. In new-born children there is often a circular fold at the *ora serrata* (*Lange's fold*). In the retina itself the rods and cones are the most delicate structures, and often show *post-mortem* changes, being swollen and fused, or broken down into a granular mass. The nuclear layers may also show irregularities owing to unequal shrinking, but these changes are less marked since formol has come into use, because of its good penetrating qualities. The nerve-fibres are often varicose, as the result of *post-mortem* changes or imperfect hardening (see “Degeneration of the Retina”).

The finer *post-mortem* changes have been studied by Birch-Hirschfeld, by Nissl's method, using thionin as the stain. The results

obtained by this extremely delicate method must be accepted with caution, as they are only strictly comparable when the minutest details of technique are kept constant. *Post-mortem* changes commence in the ganglion cells two hours after death. The pericellular space becomes visible, and the Nissl granules become slightly blurred at the edges, the smallest breaking up. In three and a half hours the nucleus shows vacuoles and commences to shrink; larger and more numerous vacuoles appear in the periphery of the cytoplasm. In five hours the Nissl granules have broken up and formed a dusty, diffuse stain, whilst the other changes have progressed. In seven hours the cells have been transformed into a mere granular mass.

The cells of the nuclear layers also show changes. In three and a half hours many of the bipolar cells are degenerating, the nuclear networks being retracted from the peripheral membrane and their nodal points thickened. The lamellation of the outer nuclei has disappeared. In seven hours the chromatin has almost entirely gone.

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WOUNDS AND INJURIES

As regards wounds of the *retina*, only one monograph of importance has been published, apart from my own work upon the subject. Doubtless many facts of importance are published incidentally in the records of the pathological lesions occurring in human eyes, but these are invariably so vitiated by concomitant factors that they possess little importance unless controlled by experimental results.

The paper referred to is one by Tepljaschin, of Kasan, published in 1894, on "The Histological Changes in the Retina after Experimental Injury." This is an exhaustive paper on the subject, and some of the deductions drawn by the author from his preparations are so at variance with current pathological ideas, and my own conclusions, that it requires somewhat detailed consideration.

The experiments were made upon rabbits, "not less than fifty experiments" having been performed. An attempt was made to wound the retina without injuring the choroid and sclera: it is improbable that this was effected in many, if any, of the cases. A dissection needle was passed through the coats of the globe 5-9 mm. behind the margin of the cornea, and a linear wound made in the retina on the opposite side. Perforating wounds were also examined, made by a Beer or Graefe knife inserted 4 mm. behind the corneal margin, a meridional section of 4-5 mm. being made. Finally, in other cases the retina

was cauterised, as in the experiments of Roth and Baquis, by an electro-cautery thrust into the globe as far as possible behind the limbus.

The animals were chloroformed to death at intervals after the operation varying from 22 hours to 285 days. For vertical sections of the retina, the tissue was fixed in Flemming's weak or strong osmic-chromic-acetic acid mixture, and cut in celloidin. Flat preparations were stained by a modification of Ehrlich's *intra vitam* methylene blue method.

Perforating wounds, and those produced by cauterisation cause an increase of the wandering cells in the vitreous, commencing on the

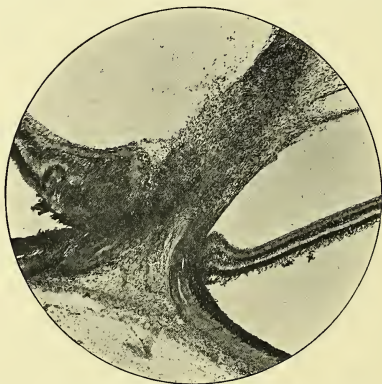


FIG. 397.—WOUND OF THE RETINA. $\times 25$.

Parsons, R. L. O. H. Rep., xv. From a monkey; wound made with a Graefe knife (fifteen days). The edges of the sclerotic are turned inwards and separated by a plug of new-formed fibrous tissue derived from the episcleral tissue. This forms the centre of a mass of more fully developed connective tissue which extends far into the vitreous, fine filaments reaching the ciliary body.

second day and reaching a maximum on the fourth or fifth. This is most marked in the immediate vicinity of the wound, but extends for varying depths into the vitreous. Are these cells entirely due to emigration from the surrounding blood-vessels, or are they, at least in part, due to division of the normal wandering cells of the vitreous? H. Pagenstecher, from experiments in which a foreign body was introduced into the vitreous, agrees with the majority of authors in regarding them as due to emigration. Hebb and Brailey, on the other hand, in a paper on "Suppurative Hyalitis," "deduce the general conclusion that the migration of the colourless blood-corpuscles bears no part in these cases of suppuration of the vitreous body." Haensell, from experimental data, holds the intermediate position regarding the increase to emigration from the retinal and choroidal vessels, supplemented by

proliferation of the normal cells found in the vitreous. Potjechin ascribes the primary increase to emigration, and subsequent increase on stronger or longer inflammation to proliferation. Wedl and Bock figure vitreous cells in different stages of direct cell-division, and the possibility of simple cell-division in leucocytes is proved by the researches of Bizzozzero, Ranvier, Klein, Stricker, Flemming, Lawdowsky, and others. That they can also increase by karyokinesis is shown by Peremeschko, Kultschizky, Marchand, Metschnikow, Schpronk, and Flemming. Further, Arnold describes increase of leucocytes by so-called "fragmentation" (an appearance similar to, if not identical with, that of the ordinary polymorphonuclear cell). Tepljaschin figures

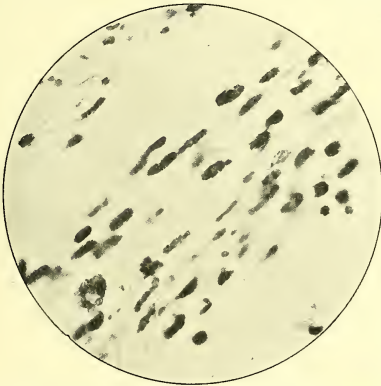


FIG. 398.—WOUND OF THE RETINA: CELLS IN THE VITREOUS. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From a monkey, fifteen days after injury. Leucocytes containing spherical pigment granules in the vitreous.

examples of each mode of cell-division, from leucocytes found in the vitreous on the fourth day after operation.

Regressive metamorphoses occur in some cells even on the first day after operation, and these become more and more patent as time goes on, so that after the fourth or fifth day, when the leucocytes tend to decrease in numbers, they become predominant. The cells now show nuclei with deeply-stained (with safranin) granules of varying shape and size, or the nuclei are broken up into small deeply-stained particles. These are doubtless forms of nuclear *débris* from dead leucocytes (karyorhexis, karyolysis). Other cells show vacuoles, others, again, fatty degeneration.

From the fourth to fifth day some of the leucocytes become grouped around new-formed fibrous tissue, which fills the perforating wound. Karyokinetic figures are seen amongst them.

Sooner or later the inner surface of the retina (internal limiting

membrane) becomes covered with flattened cells with well-marked oval nuclei. These are endothelial cells: "in flat preparations, stained with methylene blue, they are seen to be derived from wandering cells." (Tepljaschin). This appearance is familiar in pathological human eyes in many conditions, *e.g.* chronic retinitis (Iwanoff), shrunken vitreous (Duke Carl Theodor), detached retina (Nordenson), intra-ocular cysticercus (Dolina), etc.

In later stages a lamina of connective tissue often forms over the surface of the retina, "which is so intimately bound up with the retina, that the radial supporting fibres of the latter (*i. e.* Müller's fibres) pass over into this lamina and take part in its formation." (Tepljaschin). Similar structures are also seen in pathological human eyes, where

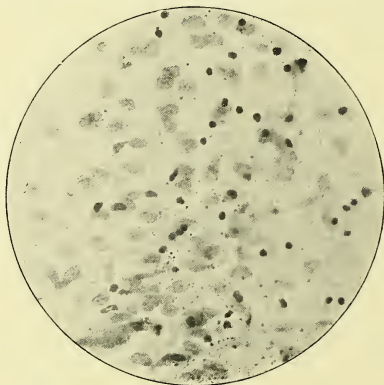


FIG. 399.—WOUND OF THE RETINA: CELLS IN THE VITREOUS. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From a monkey, fifteen days after injury. Endothelial cells (pale), leucocytes (dark), and free pigment granules in the vitreous.

they are known as retinitis proliferans (Manz), due, according to Leber, to hæmorrhages. The question arises, Can these fibrous tissue developments arise from wandering cells, or are the elements of other tissues necessary to their formation?

Much controversy has taken place in the realm of general pathology as to this question, and, whilst the transition of leucocytes into granulation tissue was formerly admitted, much doubt has been cast upon it in recent years, dating especially from the opinions expressed by Ziegler, Marchand, Grawitz, and others at the 10th International Medical Congress in Berlin, in 1890. Sherrington and Ballance¹ in the previous year published an important paper in which they practically proved that the new fibrous-tissue cells do not arise from leucocytes, but from plasma-cells which invade the injured area immediately

¹ SHERRINGTON AND BALLANCE, Journ. of Physiology, x, 1889, p. 550.

after the leucocytic invasion. These plasma cells or fibroblasts are derived from those normally present in mesoblastic connective tissues. The method used was the examination of the films of tissue invading the space ($\frac{1}{20}$ mm. thick) between two cover-glasses, which had been imbedded in the subcutaneous tissue of living rabbits or guinea-pigs for varying lengths of time from four hours to eighteen days.

As regards the eye, H. Pagenstecher's experiments were considered by him to confirm the then accepted view. Tepljaschin, using the methylene-blue method, lays great stress upon the fact that the leucocytes take up this stain, whilst the embryonic connective tissue cells do not. Many of the former are seen to arrange themselves in layers and become elongated, spindle, or star-shaped. They thus approximate

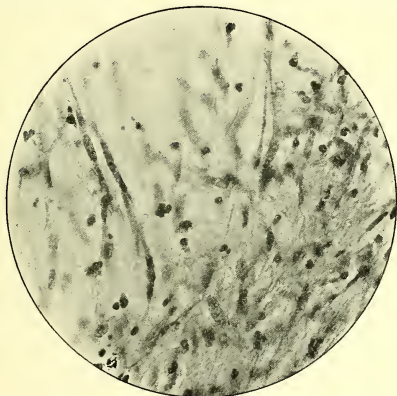


FIG. 400.—WOUND OF THE RETINA: CELLS IN THE VITREOUS. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From a monkey, fifteen days after injury. Organising connective tissue, long spindle-shaped cells with large oval nuclei; leucocytes interspersed.

the form of new fibrous-tissue cells. The same phenomenon was found to occur in a case of cyclitis; hence he concludes that "wandering cells of the vitreous can, in the latest stages after injury of the eye, and also under the influence of chronic inflammatory processes in the uveal tract, become transformed into fixed cell elements."

The behaviour in the blood-vessels is next considered. In the rabbit the large retinal blood-vessels lie on the inner side of the internal limiting membrane, the capillary vessels passing through it, but penetrating only into the nerve-fibre layer (Krause). Injury of the larger vessels was avoided in the experiments. A few days after the operation proliferation of the endothelium of the capillaries by indirect division was observed. In later stages, large, flat, mononuclear cells, with long thin processes, were seen in the immediate neighbourhood of

the vessels, apparently directly connected with their walls. Such cells are unknown in normal adult rabbits, but are found in fishes and frogs (Hans Virchow, Zimmerman), and also in the embryo (R. Virchow, Kölliker, Lieberkuhn). From flat preparations, stained with methylene-blue, Tepljaschin concludes that we have here "so-called vessel-forming cells and especially an intra-cellular process of new vessel-formation like that described in embryonic development and in inflammatory processes by Ranvier, Ziegler, etc." New vessels were not formed in the vitreous except in the case of the masses of granulation tissue filling perforating wounds.

In the early stages general retinal œdema was seen, most marked around the ganglion cells and the outer cells of the inner nuclear layer.



FIG. 401.—WOUND OF RETINA AND CHOROID. $\times 60$.

Parsons, R. L. O. H. Rep., xv. From a monkey, nineteen days after injury. Retina and choroid replaced by fibrous scar, consisting of layers of imbricated spindle-shaped cells, closely packed together (see Fig. 402).

This was seldom observed three or four weeks after operation, and was absent after one to two months.

In the nerve-fibre layer many "varicose nerve-fibres" or cytoid bodies (*v. infra*) were found, like those described by H. Müller as characteristic of albuminuric retinitis, but since discovered in other conditions. They have been investigated by Roth and Baquis. They are found from twenty-two hours after injury, and occur both peripherally and centrally to the wound, but earlier centrally the nearer the wound to the papilla. On the peripheral side of the wound they occur later than on the central side, and they also appear later the nearer the wound to the papilla. The cut ends of the nerve-fibres swell up on the central side, but this does not occur so much upon the peripheral side; hence the former are globular, the latter club-shaped.¹ No regeneration of nerve-fibres was observed,

¹ PARSONS, 'Brain,' xxv, 1902.

although the club-shaped extremity of the part united to the cell of origin is indicative of continued, if lowered vitality. Such a result was to be expected. The axons of the ganglion-cells are analogous to true intra-spinal axons, and on no reasonable hypothesis to spinal dorsal root fibres, as has sometimes been stated. These latter are represented by intra-retinal fibres, either those of the inner nuclear layer or those of the outer nuclear layer, but *which* it is difficult to say.¹ The ganglion-cell fibres belong, therefore, strictly speaking, to the central nervous system, and it is doubtful if such fibres ever regenerate. In preparations fixed by Flemming's solution black droplets were observed amongst the fibres, due to broken up myelin. These doubtless represented some medullated fibres, which occur in abundance in

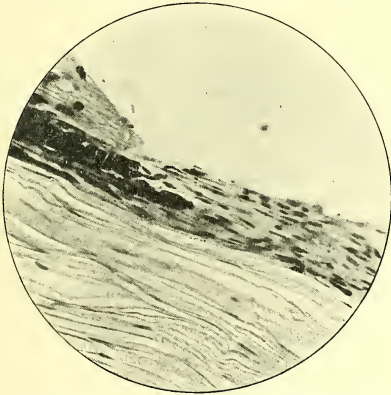


FIG. 402.—WOUND OF RETINA AND CHOROID. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From the same specimen.

the rabbit's retina. They cannot, therefore, be regarded as evidence of a fine myelin sheath to so-called "non-medullated fibres." Leucocytes were observed in large numbers around the degenerating fibres, distinguished from fixed cells by the fact that they stained with methylene blue. In late stages (194 days) ganglion-cells are found only near the ora serrata on the peripheral side of the wound, whilst, still later (285 days), both ganglion-cells and nerve-fibres had entirely disappeared peripherally. In both these cases the nerve-cells of the inner nuclear layer were intact, though they formed a thinner layer, due probably to the atrophy of the ganglion-cell processes.

In the ganglion-cell layer the changes were essentially degenerative, but appearances of cell proliferation by karyokinesis were also present. Baquis observed them also, but attributed them to a simple

¹ See PARSONS: Ophth. Rev., xx, 1901; 'The Neurology of Vision,' London, 1904.

reaction to irritation, since they were absent after seven days. Tepljaschin confirms this view, though he found many as late as the fifteenth day (most from fourth to fifth day). They were mostly in the monaster stage, and showed concomitant signs of degeneration, *e. g.* fatty degeneration, vacuolation (hydropic degeneration), etc.

The changes in the inner reticular layer were principally due to œdema, such as swelling of the fibres and invasion by wandering cells. The changes in the inner nuclear layer resembled those in the ganglion cell layer, but there were more mitotic figures, belonging probably, according to Tepljaschin, to Müller's fibres, though some undoubtedly belonged to the nerve-cells. Monasters occurred most frequently, and were also accompanied by degenerative changes. Especially note-



FIG. 403.—WOUND OF RETINA AND CHOROID. $\times 120$.

Parsons, R. L. O. H. Rep., xv. From a monkey, seventeen days after injury.
Very thin fibrous tissue scar.

worthy was the hyaline degeneration of some cells, similar to that described by Oeller in amblyopia saturnina, Hess in naphthalin poisoning in rabbits, etc. It occurs chiefly in the outer row of cells, *i. e.* where nutrition from the retinal vessels (in the rabbit) stops.

The outer reticular or internuclear layer is somewhat atrophied, owing to the disappearance of the processes of the degenerating nuclear layer cells; œdema is associated with the atrophy.

In the outer nuclear layer the nuclei are separated by œdema, the normally invisible Müller's fibres being now visible, with their oval, faintly staining nuclei often showing karyokinetic figures. The latter occur earlier here than elsewhere (2nd day, being absent after the 2nd week). Nuclear division of the nerve-cells is only seen a short distance from the wound (fourth to sixth day). After the sixth day some

of these, situated in parts where destruction is limited to the rods and cones, resemble embryonic forms of these structures. The nucleus sends out a fine process, ending in a knob, through the external limiting membrane, the process being covered by a thin layer of cytoplasm. These resemble the inner limbs of cones, with ellipsoidal bodies (Kostenitsch). The nuclear chromatin of many cells in this layer shows degenerative changes, being broken up; so that later the layer becomes thin by destruction of the cells, *débris* of which is carried into other layers of the retina.

The rods and cones are either destroyed or in an extremely degenerated condition, their place being taken by a homogeneous exudate. In places, however, elongated rods and cones were observed, such as have

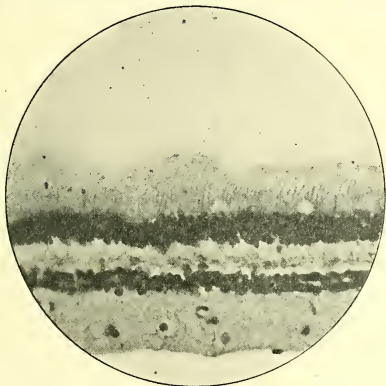


FIG. 404.—RETINA CENTRAL TO WOUND. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From the same monkey, showing thinning of the retina and diminution in number of ganglion-cells.

been described by Nettleship in secondary glaucoma, Leber in glioma, Alt in albuminuric retinitis, Nordenson in detached retina, etc.

The pigment epithelium is separated from the rest of the retina by exudate. The cells show fatty degeneration and vacuoles, though some show mitotic figures.

The following is a description of a typical aseptic wound of the retina in a monkey, examined fifteen days after the injury:

The wound passes through the retina and choroid, and just through the sclerotic. The edges of the sclerotic are turned inwards and separated by a plug of new-formed fibrous tissue derived from the episcleral tissue. This forms the centre of a mass of more fully developed connective tissue which extends far into the vitreous (Fig. 397). Anteriorly it spreads out and branches, long fine filaments spreading out as far as the ciliary body. The ciliary body is not

inflamed. The non-pigmented cubical cells of the pars ciliaris retinæ are irregularly elongated, and appear in places to have definitely proliferated. The inner ends are in contact with extremely delicate filaments made up of long spindle-shaped and branching cells, the filaments lying almost parallel to the surface, sweeping round in a wide curve towards the lens, and then back, to be lost in the mass of tissue springing from the wound. Scattered leucocytes, few in number, lie upon the pars ciliaris retinæ and pervade the new-formed tissue. They are quite typical in their appearance, though they belong to different kinds of white cells, but no appearances in any degree suggestive of transition into spindle-shaped cells are seen. Many of the leucocytes look perfectly normal, many others are obviously disinte-

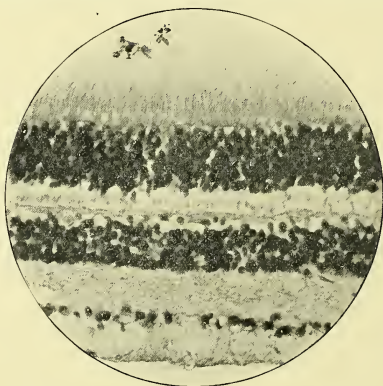


FIG. 405.—RETINA PERIPHERAL TO WOUND. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From the same monkey; the retina is normal.

grating. Many cells contain pigment granules in their cytoplasm (Fig. 398), and in places free pigment granules are abundant (Fig. 399). Most of the pigment-containing cells are undoubtedly leucocytes, and none can be definitely stated to be true pigment cells (Fig. 398). They and the free granules are especially abundant near red blood corpuscles, of which there are comparatively few in this eye, no large vessel having been wounded in this experiment. Where they occur they are usually arranged in layers between the parallel fibrous filaments: there is no evidence of new capillary formation in the anterior part of the eye.

Considering next the main mass of tissue filling the wound, the central core, pyramidal in shape, with the apex forward, derived from the episcleral tissue, contains more leucocytes than the remainder. In the centre is a widely-dilated, thin-walled new vessel, containing red corpuscles. The leucocytes and some pigment cells are most marked

near this vessel. Covering this pyramidal process of episcleral tissue are the in-turned edges of the sclerotic and choroid, outside which the very slightly altered retina is adherent. (The general detachment of the retina in the figure is due to the preparation of the specimen, and was not present when the eye was bisected.) The edges of the sclerotic can be made out in the sections, though they are rounded off and capped with fibrous tissue, which is furthest developed in this situation. The choroid spreads out and is lost in a more highly nucleated connective tissue, amongst which pigment cells are seen: these dwindle rapidly as the tissue is traced inwards. The main mass spreading out into the vitreous consists of closely packed laminae, made up of imbricated spindle-shaped and branched cells, with long oval nuclei. The tissue is most organised at the base, spreading out into processes



FIG. 406.—WOUND OF RETINA AND CHOROID. $\times 17$.

Parsons, R. L. O. H. Rep., xv. From a monkey, nineteen days after injury.

which extend far into the vitreous and consist of looser tissue of the same kind. Here the shape of the cells is most easily demonstrated (Fig. 400). Interspersed amongst the embryonic connective-tissue cells are a comparatively small number of leucocytes, recognised by the deeply stained round nuclei, and a few endothelial cells. The latter are recognised by their large oval (but little elongated) faintly staining nuclei, with deeply stained nucleoli. They are seen with difficulty in the base of the mass, where the tissue is very compact, but deeper in the vitreous they become prominent, and in places are extremely numerous (Fig. 399).

The retina still retains its layers intact, and is only slightly altered even close to the wound. Here there is slight œdema of the inter-nuclear layer. The pigment epithelium, rods and cones, and the nuclear layers are normal. The nerve-fibre layer and the vessels

appear normal, except peripheral to the wound where many of the ganglion cells have degenerated, and the nerve-fibre layer contains many round cells. These are not conspicuous in other parts of the retina.

The choroid is apparently normal except close to the wound. It is deeply pigmented in the monkey, and it is impossible to make out its finer structure without bleaching, which would have spoiled more important structures. Near the wound there is an enormous development of new fibrous tissue growing directly into the proliferating mass, which is evidently largely derived from this coat. There is no evidence that the sclerotic takes any part in this process, but this point is better demonstrated in other specimens.

The optic nerve showed degeneration when examined by the



FIG. 407.—WOUND OF RETINA AND CHOROID. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From the central part of the same specimen, showing persistent degenerated retina, covered on the inner side by layers of endothelial and other cells.

Marchi method. Degenerated fibres were scattered in small numbers over the whole transverse section, but there was a well-marked aggregation on the nasal side corresponding with the retinal wound.

In considering lesions of the retina, etc., there are certain fundamental points which must be continually borne in mind as of cardinal importance in the process of repair. The first is the question of sepsis. In aseptic experimental lesions there is scarcely any reaction, and after a day or two the eyes looked quite normal; further, there was no trace of pus in the a.c. or vitreous. The pathological cases which I have examined were probably all septic, though in varying degree or nature. There is often a clinical note that hypopyon was present at some stage. In virulent cases in which acute purulent panophthalmitis rapidly supervenes all tendencies towards repair are rendered abortive.

The second fundamental point to be held in view is the period which has elapsed between the infliction of the wound and the examination. The third point is the relative severity of the wounds in the various instances, and here many factors have to be taken into account. Of prime importance is the implication of the choroid or sclerotic, or both, in addition to the retina, for in no case are we here dealing specially with ordinary perforating wounds (except in the wounds of entry in the experiments), for even where all the coats of the eye were pierced, it was from within and not from without—a point of considerable importance. Further, the injury of any considerable blood-vessel adds enormously to the severity of the wound. The site of the wound of entry plays a prominent part, those in which it is situated in the

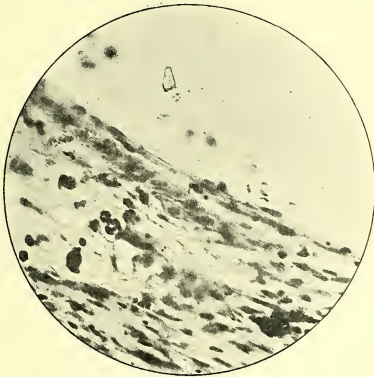


FIG. 408.—WOUND OF RETINA, CHOROID, AND SCLEROTIC. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From a monkey, eighteen days after injury, showing marked endothelial proliferation.

cornea, involving wound of the lens, leading to much more general disorganisation than when the perforation is purely scleral. The size, nature, and shape of the foreign body, its probable velocity, etc., must also be considered.

Turning now to the histological features in the healing of retinal, choroidal, and scleral wounds, we find that the process is, in its essentials, the same as in other parts of the body, but that in details it is modified by the specific characters of the tissues involved. As elsewhere there is invariably hæmorrhage followed by leucocytic infiltration (Stage 1). This is succeeded by organisation or cicatrisation (Stage 2). These stages must now be considered in the light of the data obtained, paying due regard to previous work upon the subject—both special (ophthalmic) and general.

(1) **Hæmorrhage.**—It is obvious that even the slightest wound of

the mammalian retina must be accompanied by hæmorrhage, since the non-vascular part of the retina lies between two vascular layers. In the peripheral parts the hæmorrhage may be minimal and little more than capillary. Here mere endothelial walls are ruptured, and they probably play little part in subsequent events. In all cases, however, red corpuscles and leucocytes are set free, together with the plasma which provides some, at any rate, of the precursors of fibrin. In every instance, therefore, the wound is rapidly filled with a clot, consisting of fibrin, with red corpuscles and leucocytes in its interstices. Now, the hyaloid membrane of the vitreous and the so-called internal limiting membrane of the retina have also been wounded for a corresponding extent, and the blood is thus given access to the vitreous. If a larger



FIG. 403.—WOUND OF RETINA, CHOROID, AND SCLEROTIC. $\times 28$.

Parsons, R. L. O. H. Rep., xv. From a monkey, twenty-one days after injury. A stream of fibrous tissue, derived from the choroid, passes forwards into a mass of red corpuscles lying in the vitreous.

vessel has been wounded blood is poured out in the direction of least resistance, *i. e.* along the track of the knife or foreign body. The intra-ocular tension has been lowered and in some cases nullified, but the consistence of the vitreous offers resistance to an equal distribution of the exudates. The retinal, and probably the choroidal, arteries exist normally in ideal anatomical surroundings for rapid retraction, whereby their elastic coats are able to bring their whole force to bear upon the blood-stream, and thus the outflow is minimised. Where this condition is absent, as in arteriosclerosis, etc., hæmorrhage is followed by much more serious consequences, unless, indeed, it occurs in the otherwise intact eye, where the normal intra-ocular tension affords a similar support.

There is no evidence that the red corpuscles and fibrin play any active part whatever in the subsequent events.

(2) **Leucocytosis**—(a) *The origin of the leucocytes*.—We have seen that Tepljaschin agrees with a minority of other pathologists in regarding some of the leucocytes as derived from the wandering cells of the vitreous. I myself have failed to find the vitreous play any but a purely passive part in any pathological condition, so that I have come to regard it as inert, and to look upon such terms as “shrinking of the vitreous,” etc., as implying an activity which does not exist. At the same time, only the most painstaking investigation could really prove this to be the case, and the undoubtedly great *relative* inertness of the vitreous elements is sufficient excuse for leaving this point in abeyance.

There can be no doubt that the enormous majority, if not all, of the leucocytes are derived from the vascular (both blood and lymph)



FIG. 410.—WOUND OF RETINA BY FOREIGN BODY. $\times 60$.

Parsons, R. L. O. H. Rep., xv. From a man, four days after injury. Capsule of fibrous tissue, peripheral to foreign body (a piece of steel).

channels. In some animals, the peri-vascular lymph-sheaths of the retinal vessels are conspicuous, and it is probable that their contained lymph affords its quantum of leucocytes.

As to the question whether all the leucocytes are the result of emigration, or whether those which have already emigrated divide and multiply, it is probable that the latter view is correct, but my observations give no evidence. It may be remarked that the eye is admirably adapted for the solution of this and kindred questions, all that is required being the examination of earlier specimens by specific methods directed to the particular point.

(b) *The function of the leucocytes*.—It can scarcely be doubted that this is exactly the same as elsewhere in the body in similar circumstances. (a) *Digestive*.—By their ferment action they soften and liquefy the necrosed tissues, *i. e.* those which have been killed by the severity

of the injury. The products of digestion, now in solution, are readily carried off by the lymph-stream. (β) *Mechanical*—By their aggregation and fibrin-forming process they form plugs which help to seal up the broken and contused blood- and lymph-channels. This function has also a deleterious action in impeding the flow of nourishment to the part, thus increasing the necrosis, which they further deal with by their digestive function. It also impedes the outflow of effete material, thus leading to unfavourable conditions of vitality, which also must be taken into account. (γ) *Phagocytic*—It is unnecessary to dilate upon the bactericidal function of leucocytes here, but their phagocytic activity is most easily seen in the very marked way in which they deal with the red blood corpuscles and with the blood-pigment of broken down

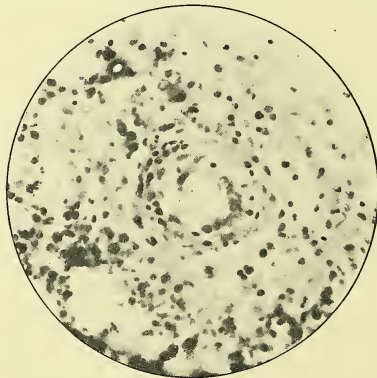


FIG. 411.—WOUND OF RETINA BY FOREIGN BODY. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From the same specimen, close to foreign body, showing persistence of a retinal vessel in a mass of leucocytes and necrotic tissue.

corpuscles (Fig. 398). This function is doubtless applied to all the more insoluble products of disintegration.

Whether the digestive activity of leucocytes is exerted upon the fibrin which they have helped to form is doubtful. One is familiar with old-standing fibrinous clots containing multitudes of leucocytes, where there is no reason to suppose that such a process has occurred, and it is probable that the fibrin is too admirably adapted for fodder for the young connective-tissue cells for it to be wasted in this manner.

(c) *The fate of the leucocytes*.—My own experiments only afford evidence of one destination of the leucocytes, viz. disintegration. This is frequently observed in the broken-down white cells, with fragmented nuclei, and in the occurrence of free nuclei.

It can hardly be supposed that this is the fate of all of them, but I

have seen no reason to suppose that they contribute directly to the formation of fibrous tissue. We have seen that the relative proportion of leucocytes to embryonic connective-tissue cells varies enormously at different periods and under different circumstances, especially sepsis, injury of the larger retinal vessels, wound of the choroid, etc. However few or however numerous they may be, they are always absolutely characteristic, and one never finds forms intermediate between them and connective-tissue cells. This is diametrically opposed to Tepljaschin's views, but it accords with the observations of Sherrington and Ballance, and of most other pathologists. It is another point which demands reinvestigation by special methods on early specimens.

There is extreme variability in the number of leucocytes found in

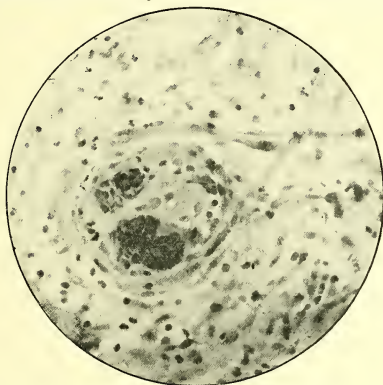


FIG. 412.—WOUND OF RETINA BY FOREIGN BODY. $\times 300$.

Parsons, R. L. O. H. Rep., xv. From a man, eight days after injury by a piece of steel. Young connective-tissue cells streaming out from adventitia of a retinal vessel into mass of leucocytes, etc.

different stages after injury in different conditions. This is a very striking point, and the most important factor seems to be the bacterial one. None of the cases described were severe cases of septic wound, but one is familiar with the rapid onset of purulent panophthalmitis in many such. Here the efforts towards repair, which we cannot doubt are exerted, are entirely abortive, and Stage 2 is never reached. The variability in number, however, is very noticeable in the aseptic cases, and seems to be largely dependent upon the severity of the wound, *i. e.* upon the injury of large retinal blood-vessels, or of the choroid, or upon actual perforation. Probably the implication of the choroid is the most important factor, and this gives some support to the hæmic origin of the cells. The more purely retinal wounds with a minimum of bleeding have very few leucocytes, but wherever there is much hæmorrhage the white cells are abundant.

We have now considered the first stage in so far as it affects the actual site of the wound. The changes in the surrounding tissues are very little marked in aseptic wounds, being limited to the ordinary signs of acute inflammation in the immediate vicinity. In septic wounds the inflammatory process is much more widely spread, resulting in congestion (most marked in the choroid), and infiltration with round cells. These changes, however, are amongst the earlier ones of which the experiments and cases offer no good example.

In the second stage the essential part of the process of healing commences and soon gains the upper hand, consisting in the formation of fibrous tissue, leading to the production of an organised cicatrix.

(3) **Cicatrization**—(a) *The formation of fibrous tissue.*—As stated

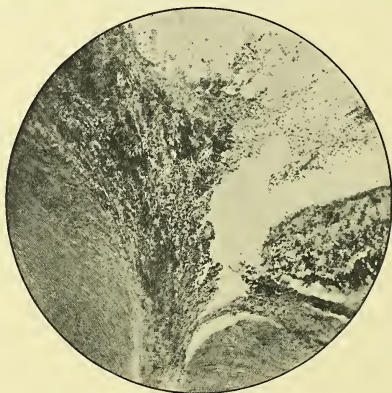


FIG. 413.—WOUND OF RETINA, ETC., BY FOREIGN BODY. $\times 60$.

Parsons, R. L. O. H. Rep., xv. From a man, eight days after injury, probably septic. Showing defective organisation, the cells being chiefly polymorphonuclear leucocytes.

above, we have seen reason to deny the formation of fibrous tissue from leucocytes. We must, therefore, look to the fixed tissue elements for the mother-cells. We are at once confronted with the number of tissues to choose from. Putting the vitreous out of the question, as before, we have in all the specimens the various structures of the retina and choroid to deal with. The true neural elements of the retina for the most part degenerate, the ganglion-cells and their nerve-fibres never regenerate, and even if the rods and cones make abortive attempts (Tepljaschin, etc.), these are merely curiosities, and form no essential part of the cicatrix. We are thus reduced to the neuroglial elements of the retina, its blood-vessels, and the choroid.

Proliferation of Müller's fibres has been described in innumerable pathological cases in human eyes; exactly how much credence is to be

attached to these cases is doubtful. The normal condition of Müller's fibres is very difficult to determine, except in isolated teased specimens. They are so overwhelmed by the nerve-cells in the normal state that only parts of them can be seen peeping out here and there. In the pathological cases the nerve elements are invariably more or less degenerated—and then Müller's fibres are said to be hypertrophied and to have proliferated. I myself have failed to find any evidence whatever of proliferation of Müller's fibres. The question cannot be said to be finally settled until it is investigated with this special aim in view, using specific neuroglial stains and examining carefully at various stages. It may, indeed, be found necessary to apply such tests to wounds in very young animals. In ordinary aseptic wounds I have not observed



FIG. 414.—WOUND OF PARS CILIARIS RETINÆ BY FOREIGN BODY. $\times 60$.

Parsons, R. L. O. H. Rep., xv. From a man, nineteen days after injury (septic). The site of wound shows œdematous and necrotic pars ciliaris retinæ, covered by polymorphonuclear leucocytes, which invade the vitreous.

such direct continuity between Müller's fibres and the new fibrous tissue such as is depicted in Tepljaschin's paper. Indeed, the differentiation between the two tissues is usually very distinct even by the ordinary methods of staining, but an apparent continuity is not infrequent in pathological specimens. Differential staining can alone determine how far the appearances are deceptive. It is perhaps *à priori* improbable that epiblastic elements should take any very prominent part in a process so essentially characteristic of mesoblastic tissues. Chemical tests may also be valuable in elucidating this point, and it would be interesting to know the relative part played by epi- and mesoblastic structures respectively in other cases of sclerosis of the central nervous system, for, as far as I know, the question has received scant attention by neurologists. It would probably be easier to decide in

these cases, and the analogy is so exact that the result would almost certainly be applicable to the retina.

We are reduced, therefore, to the mesoblastic tissues found in and around the retinal blood-vessels and in the choroid. There is ample evidence to show that both of these structures take part in the process, though the latter is by far the more important, chiefly by virtue of mere mass. The slighter the injury to the choroid, the less is the hyperplasia of connective tissue, and though no example can be adduced from the specimens examined, I have little doubt that a pure retinal lesion becomes cicatrised wholly from elements derived from its own mesoblastic elements, *i.e.* from the connective tissues in and around its vessels. Where the fibrous tissue is seen growing over the normal or degenerated retina, the choroid being intact or not in direct continuity, it is doubtless derived from the retinal vessels alone.

The persistence of the retinal blood-vessels is a striking feature even in the septic cases. When all other parts of the retina have melted away, and are replaced by masses of leucocytes (*e.g.* Fig. 411), these stand out clearly—widely dilated, often crammed with red corpuscles, or partially or completely thrombosed. The appearances seen under high magnification in these and cognate cases lead one irresistibly to the conclusion that the cells of the adventitia proliferate, and add to the mass of embryonic tissue. This is seen in an early and feeble phase in Fig. 411, and in a later and strenuous phase in Fig. 412.

Where the wound results in injury to the sclerotic no new factor is introduced, at any rate in the early stages, unless this coat is perforated, and then the episclera assists in the process in exactly the same manner as the choroid, only in less degree, due doubtless to its inferior vascularity. In anterior perforating wounds the episclera takes a larger share on account of its relatively greater vascularity here, due to its more intimate association with the extrinsic muscles. Only the fibrous tissue elements in the muscles proliferate, the muscle-fibres remaining inert.

The origin of connective tissue (and other cells) from the cubical cells of the pars ciliaris retinæ has been much insisted upon from time to time. Appearances indicating this are not wanting in my specimens, but I think they are fallacious. The cubical cells are much altered in appearance in those cases in which new filaments of fibrous tissue stretch forward through the vitreous as far as the ciliary body. Some of them are stunted, whilst others, often forming groups, are much elongated, so that they become cylindrical. The inner ends of these elongated cells are always attached to the fibrous filaments, and their elongation is probably due to traction. By the time the filaments have reached so far forwards the posterior mass of new tissue is commencing to shrink—a characteristic common to all cicatrices—and thereby considerable traction is exerted upon the anterior attached ends. The sweeping curves of the filaments are probably conditioned by the effect of the track of the wound in the vitreous upon its normal structure, and results in the ciliary retinal cells being more often drawn forwards and inwards than directly inwards or inwards and backwards.

Having stated so much, it still remains to be shown which of the mesoblastic tissue elements provides the actual mother-cells of the new formation. The specimens provide little evidence for proving this point, one of the most difficult in pathology. Attention may be directed especially to the work of Sherrington and Ballance upon the subject (*v. supra*).

(b) *The behaviour of the endothelial cells.*—Endothelial cells are found normally only in the blood and lymph-vessels of the retina and choroid, with the possible addition of an incomplete layer lining the hyaloid membrane, and a layer in the choroid which is probably a vestige of the tapetum. It is certain that they proliferate during the repair of wounds and in other pathological conditions. They are most commonly met with in various inflammatory conditions, as a uni- or multi-cellular layer covering the inner surface of the retina. In such cases they may well be derived from the cells lining the hyaloid, but this is purely hypothetical. They seem to vary greatly in numbers and distribution in different wounds, and it is difficult to assign the reasons for this peculiarity. They are generally present amongst the embryonic connective tissue, particularly in the early stages. They are not infrequently present also in later stages, and in very chronic inflammatory conditions. I have not seen such evenly arranged layers over the retina in the case of wounds as in other pathological states, but they are recognisable amongst the fibrous tissues in Figs. 407 and 408.

It has been stated that the endothelial cells become changed into new fibrous tissue, and that this is their main function in these cases. I have not seen any evidences of transition states, the two types of cells being usually quite characteristic. I believe it is not yet definitely settled which layer of the embryo they originate in, so that their development does not assist us in determining their probable destination. It is probable that their function in pathological conditions has not, in the past, received the attention it merits.

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INFLAMMATION AND DEGENERATION

The retina is a specially differentiated part of the central nervous system. Throughout this system inflammatory symptoms are but little marked anatomically, being principally confined to the vascular structures conveying nutrition. The nervous tissues themselves readily undergo degeneration as the result of the impaired nutrition, and the extensive degenerative changes which occur mask the less obvious

inflammatory ones. Hence it is important to consider the degenerative changes at an early stage, for some of the forms of so-called retinitis are essentially degenerative.

INFLAMMATION

The purely inflammatory changes include (1) vascular changes—exudation and œdema, infiltration, and hæmorrhage; (2) proliferation—of the mesoblastic tissue of the vessel-walls, and of the neuroglia. Of these the first group are most marked in acute inflammations, the second in the more chronic; but both are invariably present.

Vascular changes.—The *œdema* which occurs in the retina as the result of inflammatory exudation cannot be accurately gauged in ordi-



FIG. 415.—ŒDEMA OF THE RETINA. $\times 145$.

From the same specimen as Fig. 192, vol. i. Note the cystic spaces in the inner nuclear layer and the outer reticular layer; also the endothelial membrane on the inner surface of the retina.

nary sections, owing to the dehydration which they undergo during preparation. Evidence of it remains in the spacing out of the tissues. Thus, in the nerve-fibre layer, where the naked axis cylinders are separated from one another only by potential spaces, these become visible. This layer suffers first and most severely owing to the presence of the blood-vessels from which the fluid is derived. The neighbourhood of the disc suffers most, as the nerve-fibre layer is thickest here. In the ganglion-cell layer the same occurs, the spaces in which the cells lie becoming distended with fluid, so that the cells now no longer fill the cavities. In the nuclear layers the cells are more closely knit together, but even here they show a tendency to separate in vertical columns,

following the direction of the supporting Müller's fibres. The œdema is more manifest in the internuclear layer, where the fluid collects and presses both the nerve-fibres and the more resistant Müller's fibres apart; spaces are thus formed which may be quite large, amounting to oval cysts (Fig. 415). Their development leads to local pushing aside of the nuclear layers *en bloc*, so that these become distorted, irregular in thickness and outline. Owing to the resistance of the sclerotic on the outer side the swelling here aggravates the distortion produced by the œdema of the nerve-fibre layer; the inner layers of the retina are not only pushed bodily inwards towards the vitreous, but the inner surface is rendered wavy and uneven. Henle's fibre-layer especially suffers, and this is naturally most obvious where the layer is



FIG. 416.—CYSTIC DEGENERATION OF THE RETINA. $\times 55$.

From the same specimen as Fig. 415. Retina close to optic disc; there is a hæmorrhage in the nerve-fibre layer to the extreme left. Note separated membrane, probably hyaloid, on inner surface.

thickest, viz. at the macula. The bodies of the rods and cones readily absorb water; they become swollen and homogeneous, breaking down into spherical droplets and eventually forming a granular *débris*. The whole layer may become separated from the external limiting layer, so that its surface is wavy or even folded (Leber).

œdema of the nerve-fibre layer may pass off without leaving any permanent damage, but when the internuclear layer is involved permanent injury results. The outer layers are, however, only affected late (Dolganoff). The distortion of the layers may then be very marked, so that they are widely separated from one another in places, whilst in others they run together and become indistinguishable (Fig. 416).

Œdema not infrequently causes rupture of the external limiting membrane, so that nuclei from the outer nuclear layer escape and fall forwards into the rod and cone layer. Nuclei are occasionally found in this situation normally, but they are then few and isolated (*v. p. 543*); when caused by œdema they are present in considerable numbers, usually in columns.

In purely inflammatory conditions the amount of fluid exuded is small, so that true cysts are seldom formed; this only occurs when there is some additional obstruction to the lymph flow (*v. infra*).

The fluid poured out is richer in albuminous constituents than the normal lymph; the proteids are precipitated by the reagents used in hardening, and appear as granular deposits. These may be so small

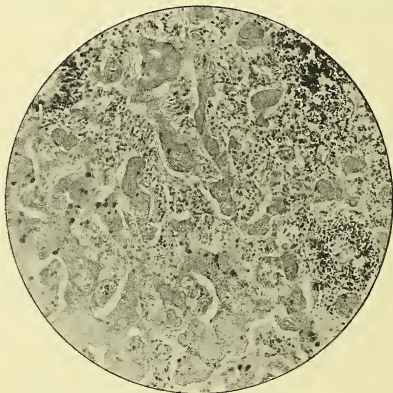


FIG. 417.—EXUDATES IN RETINA. $\times 90$.

From a photograph by Coats. From a patient with thrombosis of the central vein. The section is very oblique (almost flat); the dark dots on the left are inner nuclear layer; those on the right, outer nuclear layer.

in quantity as to be scarcely noticeable, or they may pervade the tissues (Fig. 417). In the latter case they are liable to undergo further chemical changes, forming homogeneous, hyaline globules or clumps. The fluid may coagulate, with the formation of a fibrinous network, which shows up well with Weigert's fibrin stain. It forms most readily in Henle's fibre-layer, and is therefore best seen in the region of the macula.

The exudates are eventually either absorbed or organised. In the former case polymorphonuclear leucocytes assemble round the clumps and invade them, ultimately destroying them by phagocytosis. The larger exudates are partly absorbed, partly organised and replaced by fibrous tissue, and partly degenerate. The degenerative changes are fatty and calcareous, and cholesterin crystals are also formed.

The *infiltration* which occurs in the retina in inflammatory conditions does not differ from that elsewhere. In acute inflammations the cells are derived almost entirely from the blood-vessels, the walls of which, as well as the perivascular spaces (Fig. 327), become pervaded with polymorphonuclears. The vessels thus become very rapidly surrounded by a mantle of leucocytes. In the later stages these wander further afield, most following the direction of least resistance into the vitreous. Others invade the deeper layers of the retina, which in septic cases quickly becomes necrotic.

In the more chronic forms of retinitis the infiltrating cells are chiefly lymphocytes. They also accumulate in the perivascular spaces, and later wander into the outer layers; here, in ordinary sections, they are distinguished with difficulty from the retinal cells.

The disorganisation of the walls of the vessels in severe inflammation of the retina not only gives rise to extravasation of plasma and leucocytes, but also frequently to *hæmorrhages*. These vary in degree, from microscopic collections of red corpuscles to extensive hæmorrhages, more or less filling the globe. The latter are commonly associated with widespread disease of the vessels—arteriosclerosis—or general toxæmia, nephritis, etc. They also occur as part of the necrosis accompanying septic retinitis. The larger hæmorrhages may be limited by the hyaloid membrane, as in the typical subhyaloid hæmorrhage, or they may burst through into the vitreous, tearing up and destroying the retina, and forcing the vitreous and lens forward, thus causing a secondary glaucoma. Hæmorrhages similar to those due to retinitis are brought about by many other causes, *e.g.* thrombosis of the central vein; these will be considered elsewhere.

The smaller hæmorrhages are at first limited to the nerve-fibre layer, and are often arranged along the larger vessels. It is probable that they do not necessarily arise from the vessels near which they lie, but that the blood collects in or around the perivascular lymph-sheaths, being drawn into this situation by the prevailing lymph flow. The characteristic flame shape is largely due to the anatomical disposition of the nerve-fibres. When larger, the blood spreads out laterally, only involving the nuclear layers when the hæmorrhage is considerable. Blood may, however, be extravasated primarily in this situation, but usually only when most of the hæmorrhages are in the nerve-fibre layer. In adults the blood shows a tendency to follow the direction of the supporting Müller's fibres in the outer layers; this is partly due to the normally greater resistance of these fibres, partly to their hypertrophy by the general cause (*e.g.* nephritis) which gives rise to the hæmorrhage (Leber). In newborn children Müller's fibres are delicate, and offer little resistance compared with the reticular layers, hence the blood also extends laterally here (Naumoff).

More extensive hæmorrhages tear up the retina and destroy it, necrosis, shown by feeble nuclear staining, extending beyond the area actually involved. The blood lifts up the hyaloid membrane pushing the vitreous before it. In most cases which come under microscopical examination the hyaloid is torn, and the blood invades the vitreous. When this is not extensive the blood spreads out laterally,

occupying the peripheral layers of the vitreous. Here it acts as a foreign body, part being slowly absorbed, whilst the remainder becomes encapsuled. The irritation set up by the clot causes the cells of the adventitia of the vessels to proliferate; they grow over the clot, forming first a thin membrane, composed of a single layer of endothelial cells. Later, the membrane may become thickened by the addition of young, spindle-shaped, connective-tissue cells, which finally organise into dense fibrous tissue in the usual manner.

In many cases the extravasated blood shows little tendency to clot, so that little fibrin is formed. There is generally only a small amount of granular material, due to precipitation of the proteids by the hardening reagents. Often the red corpuscles run together into a homogeneous mass, their circular outlines being lost. Absorption probably takes place almost entirely through the agency of phagocytic leucocytes, so that it is a lengthy process. The hæmoglobin is most resistant; it slowly changes into a black pigment, which for a long time retains its iron constituent. During this period it can be proved to be a hæmatogenous pigment by giving the characteristic reactions for iron (*v. p.* 515), and also by not becoming bleached by the ordinary bleaching reagents. Subsequently it loses its iron without changing in appearance; it cannot then be distinguished chemically from autochthonous pigment. A fallacy arises in the diagnosis of hæmatogenous pigment from the fact that iron is frequently taken up by the pigment epithelial cells, especially when these have desquamated (*v. Hippel*). Indeed, the iron may become widely diffused, especially in the elastic tissues of the vessel walls, the membrane of Bruch, etc. (*Ginsberg*), but this is rarely so marked as in true siderosis bulbi.

The pigment is seen particularly round the vessels, partly because much of it is formed in this situation, but also because it tends to accumulate here. In this manner the picture of retinitis pigmentosa may be very accurately simulated. Hæmatoidin crystals have rarely been found in old retinal hæmorrhages.

NAUMOFF.—*A. f. O.*, xxxvi, 3, 1890. *V. HIPPEL*.—*A. f. O.*, xl, 4, 1894. *ISCHREY*.—*A. f. A.*, xli, 1900. *DE SCHWEINITZ AND SHUMWAY*.—*T. Am. O. S.*, 1901.

Proliferative changes.—The proliferative changes in the *vessel walls* are identical with those occurring in wounds of the retina (*q. v.*). They are most marked in the less acute types of inflammation, and may be absent in virulent septic conditions.

There are also other, more specific, new formations caused by proliferation from the vessels. The most interesting of these is a membrane composed of a single layer of endothelial cells upon the inner surface of the retina (*Figs.* 415, 418). This was first described by *Iwanoff* (1865) in chronic retinitis. *Duke Carl Theodore* (1879) found a similar membrane on the internal limiting membrane, and in places on the surface of the detached vitreous in an eye with chorio-retinitis and glaucoma. *Nordenson* (1887) found a single layer or several layers of cells with oval nuclei on the inner surface of a retina detached from high myopia; here and there were isolated endothelial cells. *Dolina*

(1889), in an eye with a cysticercus, found a large-celled granulation tissue in the same situation; there were also giant-cells, formed apparently from fusion of epithelioid cells. Tepljaschin (1894) described an endothelial membrane, as well as definite connective-tissue membranes, on retina which had been injured experimentally; he thought that they were formed from leucocytes, an opinion which cannot be accepted. Krückmann (1896), also in experimental wounds, noticed the same structures, which he derived from the endothelium of the limiting membrane; it is not proved, however, that endothelium occurs normally in this situation. Finally, Groenouw (1898) found layers of endothelium on the inner surface of the retina and around the vessels in a case of flat sarcoma of the ciliary body (*see* Vol. I, p. 372); as the growth was undoubtedly an endothelioma the proliferation was probably not simply inflammatory.

These delicate endothelial membranes are not very uncommon in eyes which have been subjected to prolonged inflammation of a low

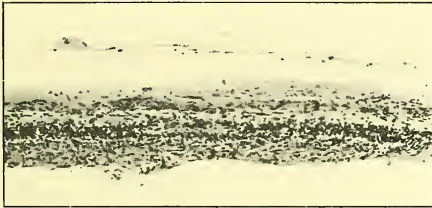


FIG. 418.—ENDOTHELIAL MEMBRANE ON RETINA. $\times 70$.

From the same case as Fig. 329. Note that the endothelial cells are elongated into spindle cells.

type, *c. g.* in old blind eyes and shrunken globes. They have rarely been observed ophthalmoscopically, when they appear as extremely delicate veils, like those produced by persistence of the connective tissue around the hyaloid vessel near the disc (Parsons) (Fig. 330). They consist of large flat cells, spindle-shaped in section, with oval nuclei; the outlines of the cells are often indefinite. Not uncommonly several layers of such membranes are seen; these easily separate from one another, but the individual membranes are fairly resistant, so that they may be removed over considerable areas without breaking. They often seem to pass into the internal limiting membrane, which is usually broken, but their true origin is seen where they unite with the adventitia of the vessels.

The inner surface of the retina is often wavy under the membrane, which then generally spans the concavities; these may contain leucocytes, clumps of pigment, etc. The wavy outline of the retina is frequently hyaline, forming a membrane resembling lens capsule; this is really hyaline fibrous tissue laid down upon the limiting membrane,

which is no true membrane, but only the expanded bases of Müller's fibres. The hyaline substance stains red with van Gieson, like ordinary fibrous tissue, and it fades off gradually at each end into other inflammatory products. It will be seen that these endothelial structures are quite independent of both the internal limiting membrane and of the hyaloid membrane of the vitreous, neither of which are cellular.

Besides these evascular membranes granulation tissue often forms in and upon the inflamed retina (Fig. 419). It obviously springs from the adventitia of the vessels which provide the young blood-channels. The disc and its vicinity contains the largest amount of mesoblastic tissue present in the retina, and it is in this neighbourhood that granulation tissue is most frequently formed (*cf.* "Retinitis Proliferans");



FIG. 419.—DEGENERATION OF THE RETINA, ETC. $\times 8$.

From a man, æt. 75, with glaucoma and hypopyon ulcer. The retina is enormously thickened by deposits of hyaline material, which is partially organised. The deep optic cup is filled with fibrin and organising exudate. The optic nerve is atrophic, and the vaginal space widely dilated.

it is not limited to this region. The young cells invade and replace the inner part of the nerve-fibre layer, force aside the Müller's fibres, and spread over the vitreous surface. The tissue is at first very cellular, spongy, and vascular; later it contracts and organises into fibrous tissue. Only rarely, as in the case of wounds and in so-called retinitis proliferans, is the vitreous involved to any considerable extent. In rare cases the granulation tissue may contain giant-cells, even in the absence of syphilis or tubercle; they are usually associated with cholesterin (*e.g.* Cramer and Schultze) or some other irritant acting as a foreign body (Fig. 334). Nodules of lymphocytes have been observed in the new-formed tissue (Landsberg).

The granulation tissue or organised fibrous tissue found between



FIG. 420.—FOLDING OF THE RETINA. $\times 11.5$.

From a child, æt. 4. December 1st, 1899.—Membranous conjunctivitis, necrosis of cornea. November 23rd, 1900.—Excision of shrunken globe. Retina folded in neighbourhood of disc.



FIG. 421.—CYSTIC DEGENERATION OF THE RETINA. $\times 55$.

From the same specimen as Fig. 303. The retina has been dragged into the glaucoma cup, where it is folded and cystic. (Parsons, T. O. S., xxv.)

the retina and choroid, often closely associated with the former and sometimes very abundant, is for the most part derived from the choroid. By the organisation and contraction of this subretinal material the retina is sometimes thrown into folds, which may be mistaken ophthalmoscopically for tubercle or a new growth (Paton and Parsons). Similarly a glaucomatous cup may become filled with connective tissue, sometimes the result of a hæmorrhage, and this, by its contraction, may pull the retina into the cup. Two such cases have been described (Kampherstein, Parsons). In the second the cup was filled with folds of retina, which was cystic owing to the irregular traction exerted upon it (Figs. 303, 421).

IWANOFF.—A. f. O., xi, 1, 1865. LANDSBERG.—A. f. O., xxiii, 1, 1877. HERZOG CARL THEODOR.—A. f. O., xxv, 3, 1879. NORDENSON.—Die Netzhautablösung, Wiesbaden, 1887. DOLINA.—Ziegler's Beiträge, v, 1889. TREACHER COLLINS.—T. O. S., ix, 1889. TEPLJASCHIN. A. f. A., xxviii, 1894. CRAMER AND SCHULTZE.—A. f. A., xxix, 1894. KRÜCKMANN.—A. f. O., xlii, 4, 1896. GROENOUW.—A. f. O., xlvii, 2, 1898. PATON.—T. O. S., xxiii, 1903. PARSONS.—T. O. S., xxiv, 1904. KAMPHERSTEIN.—K. M. f. A., xli, 1903. PARSONS.—T. O. S., xxiv, 1904; xxv, 1905.

It is probable that far too much stress has been laid upon the proliferative changes occurring in the *neuroglia* in retinitis. So-called

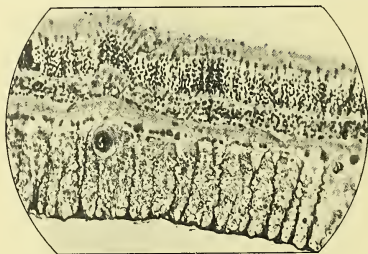


FIG. 422.—MÜLLER'S FIBRES IN THE RETINA.

Verhoeff, R. L. O. H. Rep., xv. Detached retina, stained by Mallory's phosphotungstic acid hæmatoxylin.

gliosis of the retina has been described, not only in inflammatory conditions, but even more in chronic venous congestion from heart failure, etc. (Klebs). It is also described in senile degeneration, wounds, etc. In most cases the retina is much atrophied; and there is no proof that more neuroglia is present than could be accounted for by the persistence of the normal tissue, which shows little tendency to become absorbed (Fig. 422). The condition corresponds with that which is usually termed fibrous degeneration in England. The view that the tissue which persists, and also the new-formed tissue, when any is present, is neuroglia depends chiefly on staining reactions, particularly a yellow coloration with van Gieson. These reactions are open to doubt as final criteria of tissue genesis, and the doubt is emphasised in this case by the fact that the normal neuroglia of the retina does not stain speci-

cally with many of the specific stains for the neuroglia of the central nervous system. There is an abundance of evidence that the greater part of the new-formed fibrous tissue which is found in inflamed or degenerated retinae is of mesoblastic origin, and is therefore derived from the walls of the blood-vessels or from the choroid (*see* "Wounds of the Retina"). There is no evidence that the cells of the vitreous can proliferate and produce fibrous tissue.

In the condition known as gliosis the glia-cells are said to be increased and the fibres thickened. The nuclei are increased in the nerve-fibre layer, and nuclei appear in the reticular layers, in which they are absent or scanty under normal conditions. Müller's fibres are said to be thickened, and the glia network is coarser and more obvious, especially in the inner reticular layer. This thickening is to a large extent relative rather than absolute, owing to the degeneration of the true nervous tissues. The increase in nuclei is partly relative,

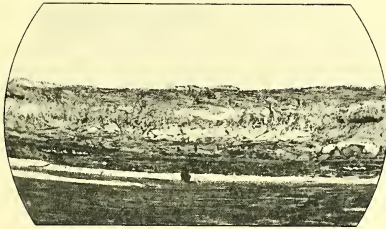


FIG. 423.—NEUROGLIA IN ATROPHIC RETINA.

Verhoeff, R. L. O. H. Rep., xv. Stained by Mallory's phosphotungstic acid hæmatoxylin.

many being remnants of the nuclear layers, but undoubtedly in part absolute, being due to infiltrating cells and others of connective-tissue origin.

Neuroglial fibres are described as streaming out into the vitreous, as in retinitis proliferans, and into the choroid, as in choroido-retinitis. In the latter case it is far more probable that the fibres are choroidal in origin, whilst in the former (q. v.) they are mostly derived from the retinal vessel walls.

IWANOFF.—A. f. O., xi, 1, 1865. KLEBS.—A. f. O., xi, 2, 1865. LANDSBERG.—A. f. O. xxiii, 1, 1877. KUHN.—B. d. o. G., 1881. FALCH.—A. f. O., xli, 4, 1895. PARSONS.—R. L. O. H. Rep., xv, 1903.

DEGENERATION

The degenerative changes affect: (1) the retinal nervous elements, (2) the neuroglia, (3) the vessels, (4) the pigment epithelium. They occur during inflammatory processes, and more especially after them, but also as the result of malnutrition and the direct action of toxic

agents. Malnutrition is usually due to interference with the blood supply, either the retinal or choroidal or both, for the retina is dependent upon both systems of blood-vessels; detachment of the retina, by placing the membrane outside the sphere of influence of the choroid, leads to malnutrition and degeneration.

The retinal nervous elements.—The *nerve-fibres*, which are the axons of the ganglion-cells and are therefore dependent upon the integrity of these cells and their continuity with them, readily undergo degeneration. In the œdematous stage they swell up and lose their sharp contours, and this usually occurs irregularly, so that patches of homogeneous material are seen, deeply stained with eosin. After the œdematous stage has passed off the fibres disappear and the nerve-



FIG. 424.—DEGENERATION OF THE RETINA. $\times 120$.

From a case of foreign body—a piece of steel—in the vitreous for three weeks. Note œdema and degeneration of the retina, and congestion of the choroid.

fibre layer becomes thinned and shrunk, or it is replaced by freshly proliferated fibrous tissue. The former condition is found particularly in the more purely degenerative and atrophic affections, the latter in the more purely inflammatory, but both are often combined in different parts of the same retina.

Much discussion has arisen as to the significance of peculiar cell-like bodies which are often found in the nerve-fibre layer in the conditions under consideration, especially in albuminuric, traumatic, and septic retinitis; they also occur in severe anæmias, papillitis, etc. They are formed principally in the posterior part, especially around the macula and disc. The bodies are round, spindle-shaped, or irregular, variable in size but often large, granular, or homogeneous, except when they contain one or more globules resembling nuclei. They are often

aggregated into clusters. The nucleoid structures are central, round, or elongated, sharply contoured, highly refractile bodies. They stain more deeply than the periphery with both nuclear and diffuse stains; they are also stained darker with Weigert's medullary sheath stain, and are dark reddish brown with van Gieson. With Russell's carbol fuchsin and iodine green stain the central bodies are bright red, the periphery bluish green.

These peculiar cytoïd bodies were first described in albuminuric retinitis by Heymann and Zenker (1856), and were regarded as degenerated ganglion-cells. This view cannot be accepted, since they occur frequently in the inner part of the layer where there are no ganglion-cells. Virchow confirmed the observation and supported the explanation. H. Müller drew attention to their uniform association with the nerve-fibres, either in the retina or papilla, and regarded them as swollen, varicose, or ganglionic nerve-fibres; he thought that they were characteristic of albuminuric retinitis, a view which was disproved by Roth. That they are not the ordinary form of varicose nerve-fibres is shown by the fact that these occur invariably as a *post-mortem* condition, and do not then present the same features. They are best demonstrated by Ehrlich's methylene blue method; perfectly fresh fibres are then seen to be smooth, whilst macerated or imperfectly hardened fibres are varicose, and may be six or eight times the normal thickness. Similar changes were observed by Tepljaschin in wounds of the retina (q. v.). Although the cytoïd bodies are not ordinary varicose nerve-fibres, it is not improbable that they may be a more pronounced form of the same condition. The phenomenon may even be due to an extremely fine myelin sheath, such as is known to be present on some nerve-fibres formerly described as non-medullated. It is likely that a naked axis cylinder does not exist, except perhaps in the small ramifications at the terminal synapse. If this view be correct the varicosity might be anticipated by analogy with other degenerating medullated fibres. The early onset of varicosity on the peripheral side (Tepljaschin) when there is an injury near the ganglion-cell from which the axon springs is probably due to shock to the cell, and is analogous to the presence of Marchi degeneration in the central ends of certain motor nerves, *e. g.* hypoglossal, when the nerve is forcibly torn out, a result which does not follow if the nerve is simply cut through (*see* "Optic Nerve"). The shock to the cell is apparently always sufficient in the case of retinal injury to lead to ultimate degeneration of the part still attached to the ganglion-cell, but is less when the wound is near the papilla, and therefore presumably far from the cell. Litten, with whom Greeff agrees, regards the cytoïd bodies as clumps of degenerated leucocytes; the latter points out that neuroglia cells are scanty in this situation, so that it is improbable that they can account for the appearances; moreover, it is unlikely that they proliferate, at any rate to a sufficient extent.

When medullated nerve-fibres are present in the retina they lose their medullary sheaths when the fibres degenerate, as, for example, upon the onset of optic atrophy (Pflüger (in rabbits), Wagenmann, Nettleship) or glaucoma (Frost).

HEYMANN AND ZENKER.—A. f. O., ii, 2, 1856. VIRCHOW.—Virchow's Archiv, x. MÜLLER.—A. f. O., iv, 2, 1858. ROTH.—Virchow's Archiv, lv, 1872. TEPLJASCHIN.—A. f. A., xxviii, 1894. PARSONS.—R. L. O. H. Rep., xv, 1903. GREEFF.—In Orth's Lehrbuch, Berlin, 1903. PFLÜGER.—Trans. Internat. Ophth. Congress, Milan, 1880. WAGENMANN.—A. f. O., xl, 4, 1894. NETTLESHIP, FROST.—T. O. S., xx, 1900.

The *ganglion-cells* are the least resistant cells of the retina, always degenerating first, followed by the inner nuclear cells, and last of all the outer nuclear cells. The principal change is the formation of vacuoles in the ganglion-cells; most of these contain fatty material. Hyaline degeneration has been described by Oeller in lead-poisoning and granular nephritis. Degenerative changes have been well depicted by Dolganoff.

Even in the early œdematous stage the ganglion cells readily



FIG. 425.—DEGENERATION OF THE RETINA. $\times 230$.

From a man, æt. 25; eye affected eighteen years, blind several months. There was a deep glaucoma cup. Note the atrophy of nearly all the layers of the retina, and the congestion of the choroid.

undergo irreparable changes. These are first indicated by the failure to absorb nuclear stains, so that under a low magnification the whole layer seems to have disappeared. With a higher magnification it is found that the pericellular space is filled with fluid; the cells are compressed so that they assume angular or crescentic forms, or they may disappear entirely, leaving the space empty. Leucocytes often invade the pericellular spaces. The cells show vacuoles both in the cytoplasm and in the nucleoplasm, as already described.

The finest changes have been investigated by Bach, and more exhaustively by Birch-Hirschfeld, by the Nissl method. The early *post-mortem* changes (*v. p.* 546), and the limitations of the method must be very carefully borne in mind in interpreting the results. Bach found that the ganglion-cells in detached retinæ showed breaking down of the

Nissl bodies, so that the cells became stained diffusely; the stained particles gradually pass more and more to the periphery of the cells and finally disappear. The unstained portion looks homogeneous, and contains vacuoles which run together; finally, the cells shrivel up and are completely destroyed. Less radical changes have been described by Birch-Hirschfeld in toxic amblyopias; these will be considered elsewhere.

The destruction of the ganglion-cells entails the degeneration of their axons, which form the main mass of the nerve-fibre layer and of the optic nerve. It is uncertain whether moderate degenerative changes in the Nissl bodies can be recovered from, but analogy with other parts of the central nervous system would render this probable. There is no evidence that advanced changes admit of recovery nor that regeneration of the cells ever takes place.

OELLER.—Virchow's Archiv, lxxxvi, 1881. DOLGANOFF.—A. f. A., xxxiv, 1897. BACH.—A. f. O., xli, 2, 1895. BIRCH-HIRSCHFELD.—A. f. O., l, 1, 1900; lii, 2, 1901; liii, 1, 1901; liv, 1, 1902.

The *inner nuclear cells* or bipolars are more resistant than the

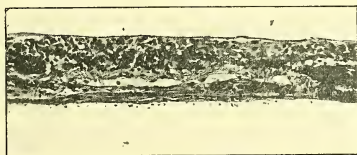


FIG. 426.—ATROPHY OF THE RETINA. $\times 120$.

From a male, æt. 21, with retinitis pigmentosa. The retina is very thin, and only remnants of the nuclear layers persist. (See Henderson, R. L. O. H. Rep., xv, 4, Case 2.)

ganglion-cells and less so than the outer nuclears. They stain more feebly normally, and this is emphasised in pathological conditions. Sometimes they stain only with eosin, whilst the outer nuclei take up the hæmatoxylin, and Verhoeff has shown that with Mallory's phosphotungstic acid hæmatoxylin after hardening in formol only the outer nuclei stain. These reactions, however, are not constant; indeed, they are the exception, yet they point to fundamental differences which are not obvious in ordinary sections.

The more marked degenerative changes in the bipolars consist in *swelling*, followed by *shrinking and breaking down*; the individual cells show various stages of feeble staining which is characteristic of necrosis. They also lose their regular arrangement, swarming out into the adjacent layers. This may be so marked that the distinction between the two nuclear layers is often lost; they run together or may even cross.

The *outer nuclear cells*, apart from their rod and cone processes,

persist longest of any cells in the retina; they can often be seen intact when no other retinal elements are recognisable.

Even the *rods and cones*, though they succumb with the greatest ease to oedematous and *post-mortem* changes, are relatively resistant to actual pathological conditions (Greeff). It is by no means infrequent to find them regular and intact in old blind eyes with glaucoma, choroiditis, etc., if the preparation of the sections has been carried out with due care. When they degenerate the changes they show are identical with



FIG. 427.—RETINAL DEGENERATION.

those found in *post-mortem* specimens (*v. supra*). They swell up, lose their striations, and finally break down into a granular detritus.

GREEFF.—In G.-S., 1900. VERHOEFF.—R. L. O. H. Rep., xv, 1903.

The neuroglia.—The Müller's fibres undergo fatty degeneration, with the formation of vacuoles, which are often arranged like a string of pearls in the processes. Fatty globules may occur free in old degenerated retinae (Parsons). The spaces from which the retinal nervous elements have disappeared give rise to *cystoid degeneration*. This may arise either with or without oedema, but is much increased in the latter case. The spaces from which the cells have gone become filled with fluid, like a sponge. The amount of fluid generally increases owing to the accompanying derangement of the blood and lymph circulations; the neuroglia is pressed apart, the finer strands are broken down so that larger spaces are formed, whilst the denser partitions are pressed together and consolidated, being probably further strengthened by some degree of glial proliferation. The cystoid spaces

are mostly to be found in the internuclear layer and inner and outer nuclear layers, especially the former.

The spaces are usually empty, but they may contain granular material, leucocytes, degenerated retinal cells, and neuroglial cells: they may also contain fibrin and blood.

Cystic spaces are very common near the ora serrata (*v. infra*, "Cysts"). The macular region is also prone to cystoid degeneration, which may occur in the absence of inflammation. It has been described in this situation in new-born children after prolonged and difficult labour (Naumoff). It also occurs here after contusions (Haab, Kuhnt, Pagenstecher), and perforating injuries (Fuchs), in degenerative

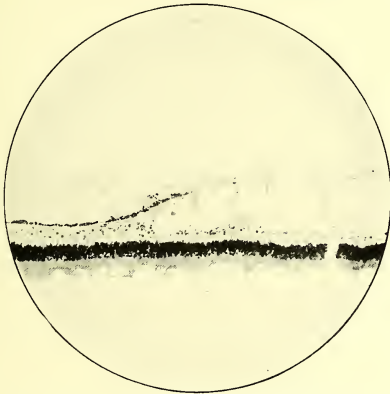


FIG. 428.—CYSTIC DEGENERATION OF THE RETINA. $\times 70$.

Parsons, T. O. S., xxii. From the same specimen as Fig. 198, vol. i. Showing cystic degeneration in the macular region.

conditions (Nuel), in syphilitic retino-choroiditis (Murakami), after injury and glaucoma (Holmes Spicer and Parsons) (Fig. 428), etc.

Kuhnt has described similar, though more irregular, cystic degeneration as a senile change. Small spaces appear between the fibres, which become rarefied and absorbed; larger spaces are also formed by the tearing of the partitions (Falchi). In this manner large sharply-defined cysts are produced, surrounded by smaller ones of various sizes. As usual, the inner and outer nuclear layers are most involved.

The cysts may grow to a very large size by the absorption of their walls, which seems to be a more or less continuous process. The inner and outer layers of the retina may thus be widely separated, and one or other wall may break down, usually the outer wall, so that the cyst communicates with the subretinal space.

It is possible that holes may be formed in the retina through the

breaking down of cyst walls; this appearance may, however, be due to cystic degeneration in the retina around a previously formed hole.

Tears in the retina are certainly facilitated by a cystic condition, *e. g.* when adhesion of the retina to the choroid has occurred at a focus of retino-choroiditis, and has been followed by detachment of the retina elsewhere.

PAGENSTECHER AND GENTH.—Atlas, 1875. LANDSBERG.—A. f. O., xxiii, 1, 1877. KUHN. —B. d. o. G., 1881; Z. f. A., iii, 1900. FALCHI.—A. f. O., xli, 4, 1895. NUEL.—A. d'O., xvi, 1896. HAAB.—Z. f. A., iii, 1900. FUCHS.—Z. f. A., vi, 1901. PAGENSTECHER.—A. f. O., lv, 1, 1902. PARSONS.—T. O. S., xxii, 1902. SPICER AND PARSONS.—T. O. S., xxii, 1902. MURAKAMI.—A. f. O., liii, 3, 1902.

The retina may appear to be much hypertrophied as the result of previous inflammation; whilst the normal layers can be distinguished,



FIG. 429.—DEGENERATION OF THE RETINA. $\times 55$.

From the same specimen as Figs. 431, 432, 441. Mass of fibrous tissue with pigment, just behind the ora serrata. It is covered by layers of hyaline fibrous tissue containing a few elongated nuclei. The dark nodule on the vitreous (upper) surface consists of red corpuscles.

they are all degenerated, and the supporting tissue is greatly increased. This has been attributed to hyperplasia of the neuroglia. It commences where the nervous elements first succumb, *viz.* in the inner layers. The supporting framework appears thickened, so that the retina looks transversely striated, an appearance which is most marked in the internuclear and nerve-fibre layers. The retina may be four or five times its normal thickness, so that the fibres are drawn out vertically. The inner surface is covered by a layer of fine fibres, which may be arranged in curves and festoons (Leber). The vitreous is adherent to the retina, and at a later stage the latter adheres to the choroid. This hypertrophy

is more apparent than real; the degeneration of the normal elements throws the framework into relief, and as this is stretched vertically without much relative distortion of the layers the quasi-hypertrophy is exaggerated. True connective-tissue hyperplasia, however, soon supervenes, the cells being derived from the vessel walls. Young spindle-shaped cells invade the interstices, and organise into fibrous tissue, which runs for the most part longitudinally and contains fewer and fewer cells. By the contraction of this tissue the retina becomes thinner than normal; all the retinal elements disappear or become unrecognisable, and the retina is reduced to a fibrous membrane containing a few blood-vessels, scattered pigment, and often cystic spaces. Hence this fibrous degeneration leads to complete *atrophy*.

Large new-formed vessels may persist in the degenerated retina. Lister considers that such vessels may account for the "angioid streaks" described by Doyne, Plange, Knapp, Stephenson, Holden, Walser, de Schweinitz, and Fretori.

DOYNE.—T. O. S., ix, 1889. PLANGE, KNAPP.—A. of O., xxi, 1892. STEPHENSON.—T. O. S., xii, 1892. HOLDEN.—A. of O., xxiv, 1895. WALSER.—A. of O., xxv, 1896. DE SCHWEINITZ.—T. Am. O. S., 1896. FRETORI.—B. z. A., xxiv, 1898. LISTER.—Ophth. Rev., xxii, 1903.

The intercellular exudates and the new-formed fibrous tissue often

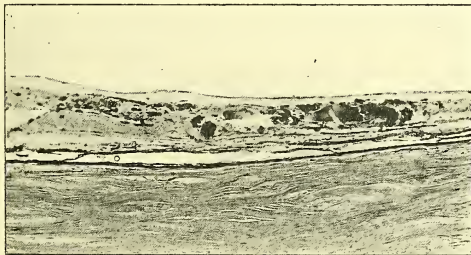


FIG. 430.—HYALINE DEPOSITS IN RETINA. $\times 60$.

undergo hyaline changes (Fig. 430). Small isolated globules and irregular clumps, the crenated edges of which show their origin by conglomeration of the smaller ones, occur in all the layers of the degenerated retina, though the larger masses are seldom seen except in the inner layers. The larger bodies may be concentrically laminated (Oeller). In staining reactions they resemble the hyaline bodies found at the disc (q. v.) and elsewhere. They rarely give the amyloid reactions (*see* Vol. I, p. 101), though such have been described in shrunken globes (Naito); usually amyloid stains give equivocal results, pointing to allied chemical constitution. Naito describes extensive amyloid degeneration of the vessel walls.

The hyaline masses may calcify. Römer found laminæ of calcareous material in the inner layers of an otherwise little altered retina in a case



FIG. 431.—FATTY AND CALCAREOUS DEGENERATION OF THE RETINA. $\times 3$.
Parsons, T. O. S., xxii. Horizontal section, showing bands in the retina.

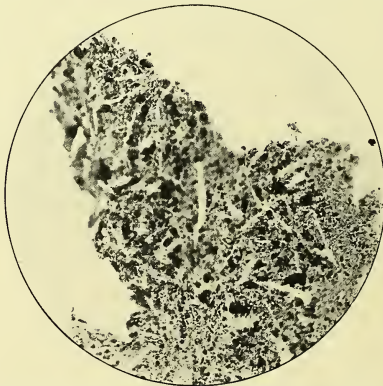


FIG. 432.—FATTY AND CALCAREOUS DEGENERATION OF THE RETINA. $\times 130$.
From the same specimen. The dark globules consist of fat, stained by Sudan III; the linear spaces were occupied by cholesterol crystals, which have dissolved out.

of albuminuric retinitis; they stained deeply with hæmatoxylin, blue with Weigert's fibrin stain, red with acid fuchsin, golden with hæmatoxylin-

orange, brown with hæmatoxylin-Bismarck brown, red with hæmatoxylin-safranin-picric acid; they did not stain with methylene blue, osmic acid, Langhan's glycogen stain, nor did they give a purple-red with van Gieson like v. Recklinghausen's hyalin. With mineral acids they gave off gas; with oxalic acid, typical calcium oxalate crystals; with ammonium molybdate a yellow colouration. They were dissolved by strong alkalies, hence they were probably a combination of calcium with an organic phosphorus base. They were attributed to calcified exudate (*cf.* "Hyaline Bodies at the Optic Disc."). These hyaline and calcareous masses must not be confounded with the "colloid bodies" of the choroid (*q. v.*), which may become free and displaced into the degenerated retina.

Diffuse deposition of calcareous salts in the form of small granules, which stain deeply with hæmatoxylin, may be observed in retinæ permeated and thickened by exudates (Parsons) (Figs. 431, 432).

OELLER.—A. f. A., viii, 1879. RÖMER.—A. f. O., lii, 3, 1901. NAITO.—A. f. O., liii, 1, 1901. MURAKAMI.—A. f. O., liii, 3, 1902. PARSONS.—T. O. S., xxii, 1902. WERNCKE.—K. M. f. A., xli, 1903, Beilageheft. PUSEY.—K. M. f. A., xlii, 1904. BAAS.—A. f. O., lvii, 3, 1904.

Ossification may occur in the retina, but only by invasion of osteoblasts from the choroid; hence it only occurs after rupture or erosion of the membrane of Bruch. The retinal tissues themselves do not ossify, but the inflammatory deposits within them. Such cases have been described by Pagenstecher, Ruvoli, Goldzieher, Schiess-Gemuseus, and others; it is not uncommon in shrunken globes in which the choroid is ossified.

PAGENSTECHEER.—A. f. O., vii, 1, 1860. SCHIESS-GEMUSEUS.—A. f. O., xix, 1, 1873. RUVIOLI.—Ann. di Ott., iv, 1877. GOLDZIEHER.—A. f. A., ix, 1880. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901.

The vessels.—The vessels in degenerated retinæ are generally much altered. The larger arteries and veins may show endovascular changes, going on to complete obliteration (*v. infra*). The walls are often hyaline (Fig. 433), and are frequently surrounded by pigment (*v. p.* 592). Calcareous particles may be deposited in the walls. Other vessels are reduced to mere fibrous cords. The capillaries may show hyaline degeneration and thrombosis. They are best demonstrated in flat preparations, when they appear as homogeneous, highly refractile strands or networks. They often look like rows of pearls, showing that globules of hyaline material have fused together. The substance gives all the reactions of hyaline material (*see* Vol. I, p. 96); it stains deeply with hæmatoxylin, less deeply with eosin, and sometimes gives an iron reaction. The capillaries may become calcified (Fig. 377).

Primary *arteriosclerosis*, as a part of general arteriosclerosis, is not uncommon in the retina, and is of considerable importance on account of its serious consequences. Here it is a question of very small vessels alone, so that the grosser changes in the media and adventitia which occur in the larger vessels of the body do not come under discussion. The process, which is a chronic inflammatory one, is characterised in



FIG. 433.—HYALINE DEGENERATION OF VESSELS. $\times 70$.

Parsons, T. O. S., xxii. From the same specimen as Fig. 428. Showing hyaline degeneration of the walls of retinal vessels; the lumen is obliterated.



FIG. 434.—DEGENERATION OF RETINAL VEIN. $\times 120$.

From a photograph by Coats. Case of thrombosis of the central vein in a woman, æt. 62. Fibrosis of connective-tissue wall, intima intact. (See Coats, R. L. O. H. Rep., xxi.)

all small vessels by proliferation of the endothelium of the intima and new formation of connective tissue, especially elastic fibres (Reimar, v. Michel, Hertel, Raehlmann, and others). According to Hertel, a constant richness in elastic fibres is the essential histological feature, but it must be borne in mind that a gradual increase in the elastic tissue is a continuous process which commences in the new-born and goes on throughout life, whether true angiosclerosis intervenes or not. It is the irregularity, both in distribution and type of the tissue, which is indicative of disease.

In the new-born child the central retinal artery or one of its larger branches, when stained by Weigert's elastic tissue stain or by acid orcein (Unna-Tänzer), already shows a well-marked line of elastic tissue in the intima; the media contains smooth muscle, with very few elastic



FIG. 435.—ARTERIOSCLEROSIS. $\times 120$.

Coats, T. O. S., xxiv. A retinal vessel showing proliferation of endothelium.

The lumen has become very greatly and eccentrically narrowed. There is no thickening of the connective-tissue wall.

fibres; and the adventitia shows extremely delicate elastic fibres. The corresponding vein contains no elastic tissue in the intima, and the media and adventitia merge together, showing a few very fine fibres. In the normal adult of 50 or 60 years of age, in the artery the intima contains a large quantity of elastic tissue, arranged in two layers under the endothelium, the outer layer staining very intensely; the media contains very delicate fibres, and the adventitia is very richly supplied. In the vein there is no elastic tissue in the intima, but a rich supply in the media, which merges into the adventitia, and this resembles that of the artery, but on a smaller scale. In subjects of 25 to 30 years of age an intermediate condition is found (Hertel).

In arteriosclerosis there is a proliferative endarteritis and to a less

degree endophlebitis. The proliferation may be uniform, so that the lumen is concentrically diminished; more commonly it is irregular, so that knob-like excrescences project into the lumen, or only one side is affected, the swelling being sickle-shaped in transverse section; sometimes both sides are affected, in which case the lumen is cleft-like. Eventually the lumen becomes completely obliterated (endovasculitis obliterans).

The swellings consist at first of cells, chiefly derived from the endothelium, partly from the connective-tissue cells. There is a superficial covering of endothelium, which is only lost at a late stage. The cells are often swollen, irregular in outline, and epithelioid in type (Raehlmann).

In more advanced cases, corresponding with the "silver-wire"

arteries of the ophthalmoscopic picture, Hertel found the endovascular changes more marked in the arteries, the perivascular in the veins. The veins rarely show the knob-like excrescences, but the adventitia is often infiltrated with round cells, an indication of the inflammatory nature of the complaint. Infiltration of the walls of the arteries is seldom pronounced. The infiltrating cells in the veins may penetrate to the intima, and the walls are often much folded.

Hertel found that there was a colossal increase of elastic tissue in the endovascular knobs and swellings. The cells, which are a prominent feature in the early stage, largely disappear. The elastic fibres in the knobs are densely felted at the outer part, becoming finer and more discrete towards the apex. They also

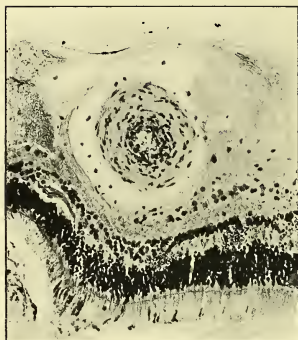


FIG. 436.—VASCULAR DEGENERATION. $\times 120$.

Coats, R. L. O. H. Rep., xvi. Retinal vein with enormously thickened wall and narrow lumen. Perivascular lymph space dilated—exudates in retina.

extend into the media, the muscle-cells of which seem to dwindle before them.

The most extensive changes were observed in the cases recorded by Hummelsheim and Leber, Raehlmann, and others. These were distinguished by widespread endovasculitis obliterans and by proliferation of the adventitia, so that the walls were enormously thickened. There were frequently miliary aneurisms on the capillaries. Sometimes the central vessels were most affected, sometimes their retinal branches. It appeared that the longer the process went on the denser became the perivascular connective tissue.

It is noticeable that marked changes are not inconsistent with normal vision and absence of ophthalmoscopic signs, the latter pro-

bably due to the fact that the changes are often most marked in the central vessels before they emerge on the disc (Hertel). The consequences of angiosclerosis are very important—thrombosis, etc.; further details will be given under these headings.

REIMAR.—A. f. A., xxxviii, 1899. v. MICHEL.—Z. f. A., ii, 1899. *HERTEL.—A. f. O., lii, 2, 1901. HUMMELSHEIM AND LEBER.—A. f. O., lii, 2, 1901. GALINOWSKI.—A. f. A., xliii, 1901. RAEHLMANN.—Z. f. A., vii, 1902. COATS.—R. L. O. H. Rep., xvi, 1904.

The pigment epithelium.—When the choroid is examined in the excised eye through the transparent retina or after the retina has become detached or has been removed, the distribution of pigment is often irregular. This is chiefly due to changes occurring in the retinal pigment epithelium. The changes accompanying “colloid bodies”—



FIG. 437.—PROLIFERATION OF PIGMENT EPITHELIUM. $\times 145$.

From the same specimen as Fig. 209, vol. i. Note the swollen cells, with sparse granules of pigment.

the white nodules which stud the choroid, surrounded by deeply pigmented rings—have already been described, as have also the changes in the pigment epithelium in old age. The latter are doubtless due in great part to pressure atrophy brought about by the hyaline concretions, which may also account for the failure of vision (Donders, H. Müller).

Other changes of frequent occurrence, resulting in a marbled appearance, or in irregular depth of pigmentation, are caused by interference with the nutrition of the outer retinal layers, which is dependent upon the choroidal circulation. This may be so extensive as to lead to widespread atrophy and depigmentation of the epithelial cells, in which case the choroidal vessels, especially the veins, are clearly thrown into relief and dominate the ophthalmoscopic picture, the intervascular choroidal pigment forming an effective background.

The effects of malnutrition upon the epithelium are twofold, local

changes and wandering of the cells; both have been exhaustively investigated by Krückmann. The local changes consist in alterations in the shape and structure of the cells. They lose their hexagonal and prismatic form, and become drawn out and spindle-shaped, or more commonly spherical and distended. The cells are larger than normal, and lose much of their pigment. In the spindle-shaped cells it is aggregated principally at the poles; in the large bladder-like cells it is uniformly distributed. The loss of pigment is due to a large amount becoming free and lying in the intercellular spaces: it may be so pronounced that the cells are recognised as pigment-cells only with great difficulty. The pigment itself is very resistant, and scattered granules and clumps are seen long after the total destruction of the cells. The

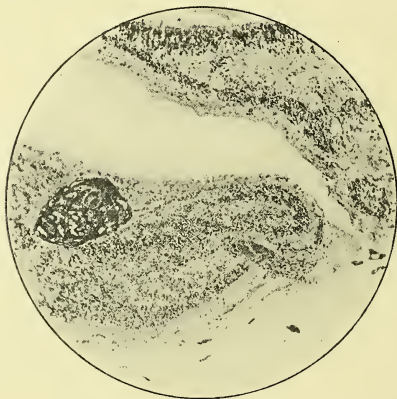


FIG. 438.—PIGMENTATION OF RETINA. $\times 50$.

From a case of chronic iridocyclitis. The pigment is aggregated around a small vessel, which is seen in the upper part.

swollen "hydropic" cells lose their close adherence to the choroid and become desquamated, lying free in the subretinal space. They generally contain vacuoles, which are often composed of fatty fluid.

There is evidence that the cells are capable of recovery if the changes have not gone too far, as shown by excessive loss of pigment. In most cases they break down and are destroyed. They are then replaced by proliferation, though nuclear figures can rarely be found. The new cells are irregular and contain little pigment, so that they much resemble the degenerating ones; they are usually, however, smaller, generally cubical or angular, and are heaped up into clumps and patches. They usually stain better than the atrophic cells.

The wandering of the pigment-cells was pointed out by Donders and H. Müller, and was confirmed by Junge, Schweigger, Maes, Leber,

and others. Berlin found that after section of the optic nerve and ophthalmic artery the retina degenerated and became pigmented. In frogs and rabbits the pigment was irregularly distributed in all the layers. Berlin considered that it was all derived from the pigment epithelium; it even wandered far into the detached retina, where it could not have been carried by the blood-stream. Wagenmann proved that the efficacy of the experiments depended, not upon section of the optic nerve, but upon section of the posterior ciliary vessels. The interference with the choroidal circulation led to proliferation of the epithelium, many of the cells of which extruded their pigment, which was carried into the retina. The new-formed cells also invaded the

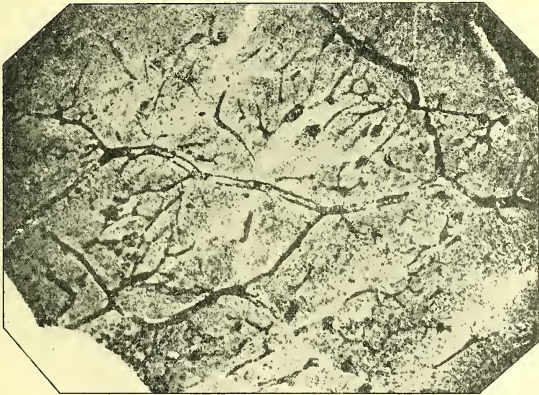


FIG. 439.—PIGMENTATION OF THE RETINA.

Lawford, T. O. S., viii. Mapping out of the retinal vessels with pigment. From a woman, æt. 23; perforating wound ten years previous.

retina, but much of the intra-cellular pigment was in leucocytes, which carried it to its fresh destination. This fact was confirmed by v. Michel.

Capauner came to the conclusion from his experiments that the pigment-cells were capable of active amoeboid movements, but this view was not generally accepted.

Krückmann made the smallest possible lesions by cutting very few posterior ciliary vessels. The results were examined ophthalmoscopically and microscopically. He found that only the new-formed pigment-cells were capable of active movement. The first stage of pigmentation consisted in throwing off of the badly nourished old epithelium, which was carried into the atrophic cystic retina. This depended upon the condition of the *membrana limitans externa*; if it was intact it prevented the invasion of the cells, but if it was patho-

logically altered and broken the cells passed freely into the deeper layers. The pigmentation only occurred where the retina was atrophic; the cells became arranged in vertical rows or in irregular clumps. The pigment shows a great tendency to become heaped up in the adventitia of the vessels and in the perivascular lymph spaces (Figs. 438-440), but it may even pass into the lumen (Bürstenbinder). The pigment is in part free, but also in cells which are round or oval or with star-like processes (Hirschberg). Krückmann regards these cells as endothelial. The invading epithelium and pigment-bearing leucocytes eventually atrophy, so that finally all the pigment is either free or contained in connective-tissue cells (Krückmann).

Besides invasion of the retina by the pigment-cells through active



FIG. 440.—PIGMENTATION OF RETINA. $\times 170$.

From a photograph by Coats. Pigmentation around a thrombosed retinal vein.

amoeboid movements, they may proliferate in such a manner as to grow into the retina, or they may be carried in by leucocytes or by the lymph-stream. All these methods occur, though in varying proportion in different cases; probably the leucocytic method is least common.

Pigmentation may occur in the absence of injury to the choroidal circulation when the epithelium is displaced from its base, as in rupture of Bruch's membrane, which may be seen in myopia (Salzmann). It may also be due to interference with the venous circulation in the choroid, *e. g.* tying the *venæ vorticosæ* (Koster and others). It occurs as the most prominent feature of most cases of retinitis pigmentosa (*q. v.*), and also after experimental or accidental introduction of foreign bodies into the vitreous (Leber), especially splinters of iron (E. v. Hippel). It not infrequently follows severe contusion of the globe, when the

picture of retinitis pigmentosa may be closely simulated (Hirsch), though the distribution is not characteristic as in the latter disease.

The pigmentation of the retina which has hitherto been described depends upon the pigment epithelium, which invades the membrane from the outer side. It may occasionally be due to invasion from within, the cells being derived from the ciliary body or iris, as in a case of glaucoma described by E. v. Hippel. The desquamated cells and free pigment are carried in the lymph-stream, mostly forwards into the anterior chamber, where they get caught in the meshes of the ligamentum pectinatum iridis (*see* Vol. I, p. 311) partly backwards into the vitreous, whence they collect on and pass into the retina. Here they



FIG. 441.—PROLIFERATION OF PIGMENT EPITHELIUM. $\times 230$.

Parsons, T. O. S., xxii. From the same specimen as Figs. 431, 432. The retina is degenerated, and towards the right is detached from the choroid. The angle between the retina and choroid is filled with proliferated, depigmented epithelial cells, which have also invaded the retina to the left.

become aggregated around the vessels, so that retinitis pigmentosa is simulated. Probably most of the pigment is in leucocytes, but this could not be conclusively proved. In flat preparations the pigment is seen to be arranged in very dark networks, which is caused by its arrangement around the vessels. This case is not unique; the condition was described by Schweigger (1859); it has since been noted by Knape, and I have also seen it.

Fatty degeneration in the cells has been proved by Ischreyt and Reinhard in a case of glaucoma.

DONDERS.—A. f. O., i, 2, 1855. H. MÜLLER.—A. f. O., ii, 2, 1856. FUCHS.—A. f. O., xxx, 3, 1884. SCHWEIGGER.—A. f. O., v, 1, 1859; ix, 1, 1863. MAES.—Jahresbericht d. Utrechter Augenlinik, 1861. LEBER.—In G.-S., v, 1877. BERLIN.—B. d. o. G., 1871. LAWFORD.—T. O. S., viii, 1883. WAGENMANN.—A. f. O., xxxvi, 4, 1890. LEBER.—Die Entstehung der Entzündung, Leipzig, 1891. CAPAUNER.—B. d. o. G., 1893. HERTEL.—

A. f. O., xlv, 2, 1898. ISCHREY AND REINHARD.—A. f. A., xliii, 1901. *KRÜCKMANN.—A. f. O., xlvii, 3, 1899; xlviii, 1 and 2, 1899. BÜRSTENBINDER.—A. f. O., xli, 4, 1895. HIRSCHBERG.—A. f. A., viii, 1879. E. v. HIPPEL.—A. f. O., xl, 1, 1894; xlii, 4, 1896; lii, 3, 1901. SALZMANN.—A. f. O., liv, 2, 1902. KNAPE.—A. f. A., xlviii, 1903. PES.—A. f. A., 1, 1904. HIRSCH.—Untersuchungen ü. d. Pigmentierung der Netzhaut, Berlin, 1905.

SENILE DEGENERATION

In old age the retina is less transparent, which accounts for the stronger ophthalmoscopic reflex. The change is due to thickening of the neuroglial elements—the limiting membranes and Müller's fibres. The vessels are often sclerosed and infiltrated with calcareous salts and granules (Leber).

Special changes have been observed, especially at the ora serrata and in less degree at the disc. In the former situation the most frequent change is peripheral cystic degeneration (*v. infra*). Apart from this there is often degeneration of the nervous elements, to which Kuhnt attributes the contraction of the field of vision in old age. The nerve-fibres, ganglion-cells, and inner nuclei atrophy, commencing at the ora serrata. The nerve-fibre layer then forms a very thin fibrous lamina, with oval nuclei, lying directly upon the membrana limitans interna; the ganglion-cells are replaced by minute spaces. The fibrous structure of the reticular layers is more plainly displayed.

Sometimes the two nuclear layers run together for a considerable distance, and are pervaded by cells and fibres of connective-tissue origin, many of the nervous constituents having disappeared. The rods and cones show degenerative changes and finally disappear. Many of these changes are to be attributed to degeneration of the choriocapillaris and the retinal capillaries. Atrophy of the choroid in this situation may lead to thinning, so that it is only one third the normal thickness.

Ultimately the whole retina here undergoes fibrous degeneration, all the nervous elements having atrophied. Slight inflammatory changes are often superposed on the purely degenerative, so that the retina adheres to the choroid and becomes pigmented, whilst the choroid contains small nodular aggregations of lymphocytes.

At the papilla fibrous tissue may insinuate itself between the retina and choroid, displacing the rods and cones outwards (Kuhnt).

Harms has investigated the senile degeneration at the macula, which was described by Haab. In this condition there are yellowish, white, or pigmented spots more or less limited to the macula, without choroiditis elsewhere. All the layers of the retina were thinned probably due to diminution in size and number of the elements as well as to their compression by disappearance of the intermediate tissues. The ganglion-cells, normally very evident here, were completely absent over an area of 0.48 mm.; this has, however, been seen in normal eyes by Kuhnt and Dimmer. The pathological changes were limited to the macula and involved the outer nuclei and the rods and cones over an area 2.4 mm. horizontally by 1 mm. vertically, corresponding with a central scotoma of 7° by 3°; the scotoma was not demonstrated clinically, but vision was reduced to fingers at 1 m. The outer nuclear layer became suddenly much thinned 1.2 mm. on each side of the

fovea; within 0.6 mm. only a few cells were present, lying close to the membrana limitans interna. The rods and cones were scanty and ill formed or entirely absent. The pigment epithelium was raised by albuminous material, the cells showing changes characteristic of choroidoretinitis. The choroid was thinned, the vessel-walls were thickened, and the choriocapillaris was particularly atrophied. There were no "colloid bodies," though these were found by Nagel in a similar case. The changes in the choroid were not limited to the macular region, so that the failure of the retina here must be attributed to "greater vulnerability" (Haab).

IWANOFF.—A. f. O., xv, 2, 1869. LANDSBERG.—A. f. O., xxiii, 1, 1877. LEBER.—In G.-S., v, 1877. KUHN.—B. d. o. G., 1881. NAGEL.—K. M. f. A., xiii, 1875. HAAB.—Korrespondenzbl. f. Schweiz. Aerzte, 1885. DIMMER.—Beitr. z. Anat. u. Phys. d. Macula lutea d. Menschen, Leipzig u. Wien, 1894. *HARMS.—K. M. f. A., xlii, 1904.

SPECIAL FORMS OF "RETINITIS"

"Retinitis" is a term which is used clinically for many conditions, only some of which are inflammatory, the others being due to œdema, hæmorrhage, degeneration, etc. It will be convenient to consider here the histology of these conditions under the designations by which they are commonly known. The retinitis of the various forms of anæmia, Bright's disease, diabetes, etc., will be considered elsewhere.

PURULENT, METASTATIC, AND SEPTIC RETINITIS

Purulent retinitis may be exogenous, or endogenous (metastatic). A form of retinitis has been described under the term "septic"; this may be an early stage of metastatic, but an identical condition is met with in other diseases, and it is uncertain what is the exact significance.

Exogenous purulent retinitis is found in panophthalmitis following perforating corneal ulcers, perforating wounds, etc. In slight cases, and in the early stage of severe ones, the inflammation is confined to the inner layers, and is due to infection from the vitreous. The tissues are pervaded with leucocytes, which are closely packed around the veins and to a less extent around the arteries. They then pass out on to the inner surface of the retina, and form cloudy masses in the outer layers of the vitreous.

The infiltration of the retina is most marked at the ora serrata and near the disc. The anterior part is specially affected because it is first attacked, and that by continuity from the ciliary body. The neighbourhood of the disc is also early attacked, probably by way of the hyaloid canal (Fuchs). The distribution of the infiltration is therefore determined by direct infection, so that, for example, the anterior part or the lower part is alone involved in the commencement. Ultimately the whole retina becomes pervaded with leucocytes in its whole thickness, and the outer layers of the vitreous are everywhere infiltrated (Fig. 442), but even then there is often more pus behind the lens and in front of the disc.

The next stage is detachment of the retina, which usually occurs

early and becomes total. It is caused by the exudation of fluid which is derived from the retina, as shown by the major aggregation of leucocytes being on the outer surface and not on the choroid. The pigment epithelium and the choroid may be normal at this stage. The detachment is further increased by the shrinking of the exudates in the vitreous; hence in the early stages the intra-ocular tension may be increased, whilst it is diminished later. The earlier the retina is detached, the less the choroid becomes involved, owing to the hindrance which the subretinal fluid presents to transmission of infection. The eye may even shrink without the choroid showing evidence of inflammation, though it is often studded with colloid bodies.

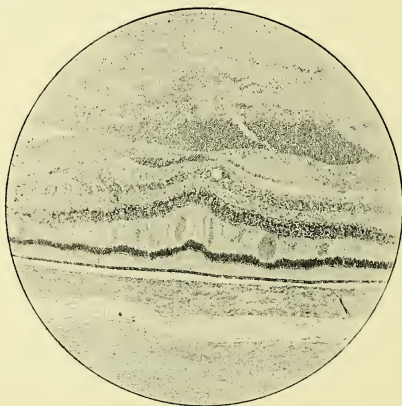


FIG. 442.—PURULENT RETINITIS. $\times 60$.

From a specimen sent by Prof. Fuchs. Panophthalmitis following a perforating wound of the cornea. Note the polymorphonuclear leucocytes in the vitreous, the coagula in the internuclear layer, and the congestion of the choroid.

If the retina is adherent at any place to the choroid, the separation of other parts may lead to ruptures. These may also be caused by necrosis at the summit of a detachment, close to a focus of pus in the vitreous. Tears are indeed generally due to necrosis at spots which are most virulently infected. If the subretinal exudation is slight the retina remains *in situ*, and the choroid is then early and extensively involved. The retina eventually undergoes complete necrosis. The leucocytes poured out are, of course, almost entirely polymorphonuclears.

Endogenous (metastatic) purulent retinitis.—Endogenous infection of the retina was described by Virchow, who pointed out that the choroid is not necessarily affected first. The disease is often bilateral, both retinæ becoming covered with thick white creamy pus. According to Axenfeld there is seldom a single large embolus containing organisms,

but generally diffuse infection of the small capillaries by finely divided septic masses. It is only possible to conjecture why the retina should be so particularly vulnerable; Axenfeld suggests the narrowness of the capillaries, associated with affections of the vessels dependent upon sepsis, such as marantic thrombosis, endothelial degeneration, septic hæmorrhage, or perhaps simple senile degeneration.

The microscopic appearances are those of exogenous purulent retinitis, perivascular infiltration, necrosis, and hæmorrhages. The vessels are often much altered (Axenfeld, Herrnheiser), showing thickening and cellular infiltration, hyaline degeneration of the media, so that arteries and veins become indistinguishable, desquamation of the endothelium, hyaline thrombosis, etc.; there may be endarteritis obliterans. Toxic necrosis of the vessel walls may be suspected when hæmorrhages occur between the nodules of purulent infiltration.

Retinitis septica (Roth).—This is a condition in which round or oval spots of considerable size occur in the retina, seldom far from the disc. According to Litten they are never found in or immediately around the macula; they have no special relationship to the vessels, but when near one may cover it. The spots may develop within half an hour (Litten). Hæmorrhages of similar form and distribution occur, but are not necessary to support the diagnosis (Greeff): they may surround the white spots, which, however, may be shown anatomically not to be due to them. The condition is not caused by embolism, and inflammatory changes may be remarkably scanty. Hence objection has been taken to Roth's designation by Litten, Herrnheiser, and others; Herrnheiser suggested the cumbersome term "retinal changes in sepsis," which is inappropriate, as similar appearances are found in anæmia, leukæmia, diabetes, scurvy, etc. Litten includes the white spots of albuminuric retinitis, and Greeff has seen them in general carcinomatosis.

The white spots have been explained in various manners. Most follow Roth in attributing them to cytoid deposits—the so-called varicose nerve-fibres (*v. p.* 578). These have been often described in them, and, doubtless, occur, though Litten was unable to find them in ten cases of septicæmia and pernicious anæmia. The nodules are situated in the nerve-fibre layer, causing prominences towards the vitreous. They consist of exudates, partly hyaline, partly granular, sometimes containing fibres, sometimes true fibrin (Litten). There is no proof that they contain fat, though it is almost certain that fatty degeneration plays a prominent part. The sections have been prepared in the ordinary methods, so that any fat present would have been dissolved out by the reagents. Fibrin must be considered a rare constituent, since it is usually found only in the hæmorrhages.

The structure of the retina is usually little changed—some œdema, and feeble staining reactions. Ischreyt has described a case with spaces in the internuclear layer, containing exudates.

The condition of the vessels offers most interest. In Ischreyt's case there was rupture of a large vein, but generally there is no evidence of rupture, and hæmorrhage has been attributed to diapedesis. It occurs in all the layers, and cannot be due, at any rate always, to septic

emboli, since cocci are seldom to be found in the retina, and there is little or no infiltration around. The capillaries near the extravasations show changes—bad staining of the endothelial nuclei, fusion of the cells themselves into a hyaline mass, sometimes varicosities, or hyaline thromboses. The large veins may be plugged with red corpuscles and leucocytes, the endothelium having disappeared, thus showing that the thrombus was *ante mortem*.

Whilst the features of retinitis septica are present in many diverse conditions, yet it is certain that they occur in some cases of true metastatic retinitis. Such cases have been reported by Goh and Grunert. In the former there were white spots and hæmorrhages in an uninfamed eye. Microscopically there were three collections of round cells, two of which contained diplococci in the centre. They were pneumococci of little virulence such as are not infrequent in the eye.

VIRCHOW.—Virchow's Archiv, x, 1856. ROTH.—Virchow's Archiv, lv, 1872. LITTEN.—B. d. o. G., 1877; Deutsche med. Woch., 1902. SCHÖBL.—A. f. A., xxi, 1890. HERRNHEISER.—Zeitschrift f. Heilkunde, xiv, 1893; K. M. f. A., xxxii, 1894. AXENFELD.—A. f. O., xl, 4, 1894. GOH.—A. f. O., xliii, 1, 1897. ISCHREY.—A. f. A., xli, 1900. GRUNERT.—B. d. o. G., 1903. STOCK.—K. M. f. A., xli, 1903. SELENKOWSKY AND WOJTECHOWSKY.—A. f. A., xlvii, 1903.

RETINITIS CIRCINATA

What is now commonly known as "retinitis circinata" was first described by Hutchinson (1876) as "symmetrical central choroido-retinal disease, occurring in senile persons." Cases were subsequently described by Galezowski (1886), Goldzieher (1887—"Hutchinson's changes"), de Wecker and Masselon (1891—"dégénérescence graisseuse"), de Wecker (1894—"dégénérescence blanche"), Fuchs (1893—"retinitis circinata"), Holmes Spicer, Fischer, and others.

The disease is characterised by a girdle of bright white spots around the macula; they lie between the temporal vessels in the part of the retina where Henle's layer is particularly pronounced. The diameter of the girdle, which is usually an imperfect circle or ellipse, or horse-shoe-shaped, is generally considerably greater than a papilla diameter. Occasionally there are spots on the nasal side of the disc (Goldzieher, de Wecker and Masselon). The spots are round, oval, or kidney-shaped, sharply defined, varying in size from fine points to the diameter of a large vessel near the disc, and these, again, fuse into larger masses. They have no trace of pigment, but there is sometimes stippled pigment at the periphery of the girdle. The spots are seldom definitely raised (Fischer, Siergiewsky). The macula near the fovea is generally greyish and slightly opaque, as though œdematous; in three cases (Fuchs, Nuel) there has been detachment of the retina here. The vessels are often tortuous and sclerosed, and hæmorrhages are the rule. These have been observed before the white spots by de Wecker and Masselon and Krülow, the former having seen the development of white spots at the sites of hæmorrhages. Fuchs found hæmorrhages in only half his cases, generally in the older ones. They are generally in the same

neighbourhood, vary in size, and often form streaks beside the vessels. Spicer found them in one case in the opposite eye, which was not affected with retinitis circinata.

Apart from arteriosclerosis—as early as *æt.* 20 in a case of Axenfeld's—the general condition of the patients is usually good; the urine is generally normal (trace of albumen—Fuchs, Goldzieher, Amann; sugar—Goldzieher; excess of urates—Siergiewsky).

The disease may be uni- or bilateral, showing in the latter case different stages of development, and occurring at different intervals of time. The patients are usually over 50: exceptions are 38 (Fuchs), 37 (Bruner), 20 (Axenfeld), 16 (Hoor) 12 (Peters); de Wecker observed the condition soon after birth and considered that it could occur during intra-uterine life. Cases have been reported in women rather more frequently than in men.

The course is chronic, the spots sometimes remaining unchanged for years. In other cases cholesterin crystals, or atrophy and pigmentation may occur, or the retina may become thickened: sometimes the spots disappear (Fuchs, Goldzieher, Krüchow). There is usually a central scotoma, which becomes absolute.

A variety of opinions have been expressed as to the nature of the spots. Fuchs considered that they consisted of coagulated albuminous exudate, similar to that found in albuminuric retinitis. He opposed the theories that they were caused by arteriosclerosis, and that they were degenerated blood-clots.

Goldzieher thought the condition caused by arteriosclerosis; the spots were necrotic, due to blocking of ophthalmoscopically invisible arterioles.

de Wecker considered that the spots were due to fatty degeneration of extravasated blood—in opposition to Goldzieher, who wrongly stated that the hæmorrhages were always secondary.

Nuel considered arteriosclerosis the cause, and Henle's layer accountable for the peculiar distribution, whilst he denied their origin in blood-clots.

The subject was discussed at the Heidelberg Ophthalmological Society in 1896. Siegrist thought the spots were deposits formed from œdematous fluid, and called the disease *œdema retinæ externum centrale*.

Only one case has been submitted to anatomical examination, by Ammann. He found hyaline masses in the internuclear layer; some of these showed very distinctly that they were derived from red corpuscles, all the different stages being demonstrable. In the crenations of the nodules there were large mononuclear bladder-like cells, filled with fat globules. Ammann thought it probable that these cells were derived from endothelium of the perivascular lymph spaces, and that they had the function of absorbing the hyaline nodules. The retina was thickened to about four times the normal in the situation of the white spots, the broadening being chiefly in the internuclear layer. The outer nuclear layer and the rods and cones were absent here, but commenced again at the margins of the spots. Müller's fibres were thickened, forming conical expansions in the nerve-fibre layer, the bases

of the cones being directed towards the vitreous. The choroid contained thickened and actually sclerosed vessels, the thickening involving the media principally. It must be stated that the eye was glaucomatous.

The evidence is insufficient to be positive that all the changes are dependent upon previous hæmorrhage. It is probable that albuminous coagula play an important part, for the resemblance to the white spots of albuminuric retinitis cannot be entirely fortuitous, and this is essentially due to œdema, and not to hæmorrhage. It will, therefore, be wise to suspend judgment until other cases have been exhaustively investigated. It must be noted, however, that the condition is not a true retinitis, but is essentially degenerative.

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RETINITIS PIGMENTOSA

Only a few cases of true retinitis pigmentosa have been submitted to anatomical investigation. The histological appearances in these cases are very similar to those found in syphilitic chorio-retinitis and other degenerative conditions of the choroid and retina associated with pigmentary changes. It is, therefore, essential to restrict this description to the undoubted cases: for, indeed, in old cases it would be extremely difficult to be certain as to the diagnosis, apart from the clinical history.

The chief feature in the pathological anatomy of retinitis pigmentosa from the diagnostic point of view is the distribution of the pigment in the retina, though cases occur in which the pigmentation is absent (Nettleship). In the early stages it is confined to a zone in the neighbourhood of the equator, so that there is an area of healthy retina both peripheral towards the ora serrata and central towards the posterior pole. As the case advances the zone becomes wider in both directions, but mostly towards the posterior pole. This pigmented zone does not include the whole of the area of retina affected. Thus in late stages, as in Lister's case, the whole retina is degenerated, and nearly the whole of it is pigmented, but there is still least pigmentation towards the ora serrata. Again, it is only in very late stages that the macular area is involved, and the limits between the nearly normal and the degenerated retina may here be very sharp (Wagenmann, Deutschmann).

The first case of retinitis pigmentosa investigated anatomically was reported by Maes. There were adhesions of the retina to the choroid, and it was evident that the retinal pigment epithelium had invaded the inner layers. This fact was insisted upon by Leber as the characteristic

feature of the anatomical basis of true retinitis pigmentosa, and it was confirmed by Landolt. Other cases have been reported by Hirschberg, Wagenmann, Deutschmann, Bürstenbinder, Greeff, Stein, and Lister, all of which are important since they show different stages and some differences of detail.

In the pigmented area it is found that the nervous elements of the retina have almost entirely disappeared; faint traces of the inner nuclear layer may be followed for a short distance here and there, but otherwise the retina has undergone fibrous degeneration. Thus the general rule is followed that the pigment epithelium only invades the atrophic retina; on the other hand, the retina is much degenerated as a rule in parts which are not invaded by pigment.

The general distribution of the pigment is best seen in flat preparations. Thus, in Lister's case, which was examined twenty years after it was first seen and diagnosed by Nettleship, the posterior two thirds were deeply pigmented, the pigmentation taking the form of an irregular network, giving rise to a speckled appearance (Fig. 443, *c*). The anterior third (Fig. 443, *b*), forming a zone about 7 mm. in width, was pale and



FIG. 443.—RETINITIS PIGMENTOSA.

Lister, R. L. O. H. Rep., xv. Strip of retina and choroid mounted on the flat. *a*. Ciliary body. *o*. Ora serrata. *b*. Unpigmented zone of retina, showing choroidal pigment and course of the choroidal vessels. *c*. Pigmented portion of retina.

unpigmented, strikingly different and sharply marked off from the posterior pigmented portion. The macular region appeared as an oval pale grey area; the pigmentation here also was much less than in the surrounding parts. Portions of the retina and choroid examined microscopically on the flat show a distinct difference in level of the retinal pigment network and the choroidal pigment, which is much paler. The black retinal pigment is distributed in two ways—in stellate patches, the processes of which intercommunicate (Fig. 444), and in lines following the course of the vessels. The paler choroidal pigment forms a background, split up by broad white lines, which correspond with the course of the choroidal vessels.

Macroscopic examination confirms the diminution in size of the retinal vessels which is so often seen ophthalmoscopically in this disease. In Lister's very advanced case the vessels were extremely minute, but with a magnifying glass the main trunks could be easily made out as white lines running over the retina; in places a very dark line down the centre of the pale path could be discerned.

The retina and choroid in this case were intimately adherent, and the choroid was adherent to the sclerotic in many places. Transverse

sections showed that only close to the disc and macula were there any traces of the normal retinal layers. The ganglion-cell layer could be well seen in the macular region, and the inner nuclear and reticular layers could be distinguished in places near the disc and macula. The rods and cones were everywhere absent, being replaced by laminated connective tissue containing numerous oval nuclei (Figs. 445, 446); this tissue lay between the pigment epithelium and the nuclear layer, the former being well marked near the macula. In sections outside the central area practically all traces of normal structure were absent from the retina. Here and there a short line of pigment cells were *in situ*, and linear groups of nuclei resembling those in the nuclear layers were seen, but the retina as a whole consisted of connective-



FIG. 444.—RETINITIS PIGMENTOSA.

From the same specimen. Pigmented portion of retina and choroid mounted on the flat; higher magnification. The darker retinal pigment is easily distinguished from the paler choroidal. The retinal pigment is arranged in lines, following the course of blood-vessels, and in patches. The white lines between the areas of choroidal pigment mark the course of the choroidal blood-vessels.

tissue, loose and reticular towards the inner side, laminated and much denser towards the outer side (Figs. 445, 446).

The fibrous tissue contained blood-vessels with thickened and deeply-pigmented walls; in most the lumen was blocked (Figs. 445, 446). Some of the walls were laminated, others hyaline. The pigmented vessels were not the main trunks, nor were they capillaries; probably they were chiefly small arterioles.

In the outer part of the retinal fibrous tissue were a few irregular excrescences from the choroid, which were pigmented, and probably derived from the lamina vitrea; the latter, however, could not be made out. The choriocapillaris was absent, and the whole choroid atrophic, but the walls of the vessels were not thickened.

In less advanced cases than that now described the degeneration is most marked in the outer layers of the retina, *i.e.* those dependent upon the choroid for their nutrition. The pigment epithelium shows partial destruction, whilst elsewhere it proliferates, forming groups of swollen cells, poor in pigment, such as are often seen in other conditions. Colloid bodies have been frequently described ophthalmoscopically, and occasionally there have been hyaline bodies at the disc (q. v.). The former have seldom been found in the cases examined anatomically, and the latter never. The pigment may become clumped amongst the remnants of the rods and cones, but cannot penetrate the inner layers until the *membrana limitans externa* is broken through. The retina may be practically normal beyond the pigment zone as well as in and around the macula. There are no signs of inflammation—infiltration with round cells, etc.—so that the condition must be regarded as a purely degenerative one; Bürstenbinder's case is an exception, but here there was a perforated corneal ulcer and purulent irido-cyclitis.

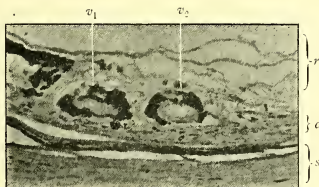


FIG. 445.—RETINITIS PIGMENTOSA.

From the same specimen. Vertical section through retina (*r*), choroid (*c*), and sclerotic (*s*). The retina is atrophied, its place being taken by connective tissue, which is loosely arranged internally, and laminated externally. Pigmented vessels (*v*₁ *v*₂) are seen in section; the lumen is blocked in both.

The changes in the choroid are of great interest from the point of view of pathogenesis. In some cases the choroid is apparently normal; but generally there are marked sclerotic changes. More or less atrophy in the choriocapillaris is almost universal, but its distribution varies greatly in different cases. Often the other vessels are much thickened and sclerosed. Wagenmann found proliferation of the intervascular stroma, and a homogeneous bone-like patch under the lamina vitrea at the posterior pole.

In Greeff's case in the affected zone both retina and choroid were completely atrophic. The retina contained no nervous elements, and consisted of fibrous tissue with elongated nuclei; all the vessels showed hyaline thickening and many were blocked. The pigment filled the perivascular lymph spaces of the large vessels in the nerve-fibre layer, and also pervaded the whole thickness. The choroidal vessels were markedly sclerosed, and there were numerous colloid bodies.

Fuchs's *atrophia gyrata choroideæ et retinae*, which has not been examined microscopically, differs from retinitis pigmentosa only in the

excessive choroidal atrophy: night blindness, heredity, and consanguinity of parents are all present in this disease (Cutler, Fuchs, Levinsohn).

There is no microscopical examination on record of retinitis pigmentosa sine pigmento (Nettleship).

Many theories have been brought forward to account for the disease. That most generally accepted predicates a primary choroidal degeneration. This is supported by the choroidal degeneration and sclerosis of vessels which are present in most of the cases; even in the cases where it is stated to be absent a low degree may have been overlooked. Thus, in Lister's case, though sclerosis of the vessels was little marked, yet it could scarcely have been entirely absent in a patient *æt.* 60, on the grounds of age if on no other. This theory explains the degeneration of the outer layers of the retina in the early stages—in fact, this is explicable on no other theory. Wagenmann's experiments show conclusively the dependence of the outer retinal layers upon the choroidal

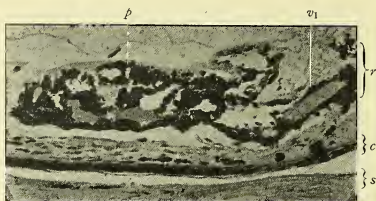


FIG. 446.—RETINITIS PIGMENTOSA.

From the same specimen, showing a similar section to Fig. 445, *v1*. A pigmented vessel cut longitudinally. *p*. One of the larger pigmented patches seen in Fig. 444.

circulation. Thus section of posterior ciliary vessels, without injury of the central retinal vessels, in the rabbit led to degeneration and pigmentation of the outer layers of the retina over the part of choroid supplied by those vessels, whereas division of the central retinal vessels alone left the outer layers intact (*v.* p. 593).

As to the cause of the choroidal degeneration Gonin and Nettleship have conjectured that it may be due to deficient blood supply, brought about by the meeting of the terminals of the posterior ciliary and recurrent anterior ciliary arteries. This meeting may be supposed to tend towards a certain amount of stasis in the zone of distribution, *i. e.* in the zone which is specially affected in retinitis pigmentosa.

Other authors consider the condition due to a primary retinal degeneration. Primary disease of the retinal vessels does not explain the facts. Lister considers that the concentric defect corresponds with a nerve distribution rather than a vascular distribution, but there is no evidence in favour of such an accurate zonular distribution of the optic nerve-fibres in the retina.

MAES.—Jahresbericht d. Utrechter Augenklinik, 1861. LEBER.—A. f. O., xv, 3, 1870; In G.-S., v, 1877. LANDOLT.—A. f. O., xviii, 1, 1872. HOSCH.—K. M. f. A., xiii, 1875. PONCET.—Ann. d'Oc., lxxiv, 1875. HIRSCHBERG.—A. f. A., viii, 1879. ALT.—A. of O., viii, 1879. NETTLESHIP.—T. O. S., xvii, 1887; R. L. O. H. Rep., xi, 1887. WAGENMANN.—A. f. O., xxxvii, 1, 1891. DEUTSCHMANN.—B. z. A., iii, 1891. BÜRSTENBINDER.—A. f. O., xli, 2, 1895. CUTLER.—A. f. A., xxx, 1895. FUCHS.—A. f. A., xxxii, 1896. LEVINSOHN.—A. f. A., xxxviii, 1899. GONIN.—Ann. d'Oc., cxxviii, 1902. STEIN.—A. f. O., lvi, 3, 1903. GREEFF.—In Orth's Pathologie, Berlin, 1903. LISTER.—R. L. O. H. Rep., xv, 1903. NETTLESHIP.—R. L. O. H. Rep., xv, 1903. AUBINEAU.—Ann. d'Oc., cxxxi, 1903. HIRSCH.—Untersuchungen ü. d. Pigmentierung der Netzhaut, Berlin, 1905.

CHOROIDO-RETINITIS

The dependence of the outer layers of the retina for their nutrition upon the choroid has already been mentioned. The affection of the

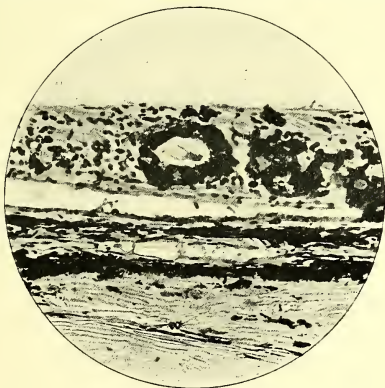


FIG. 447.—CHOROIDO-RETINITIS.

Showing appearances similar to those found in true retinitis pigmentosa.

retina, starting in the outer layers, but going on eventually to complete fibrous degeneration, accompanying choroidal disease, has been described. It is well marked in disseminated choroiditis, which indeed gives rise to conditions indistinguishable from some forms of choroido-retinitis. On the generally received theory of retinitis pigmentosa, again, this disease must be looked upon as a choroido-retinitis, using that term in the broad sense in which retinitis is usually employed, *i. e.* including both true inflammatory and degenerative conditions.

Appearances almost identical to those of retinitis pigmentosa are not infrequently found in blind eyes, generally glaucomatous ones which have been removed on account of pain (Fig. 447). Some of these are doubtless advanced cases of syphilitic choroiditis, sometimes of the typical disseminated type; others are due to extensive atrophic changes occurring in the choroid, with sclerosis of the choroidal vessels.

Any affection which involves atrophy of the choriocapillaris inevitably causes atrophy of the outer layers of the retina. The importance of Wagenmann's experimental researches must again be insisted upon here (*v. p. 593*). The atrophy of the retina need not be confined to the outer layers, for the same causes which induce choroidal atrophy may

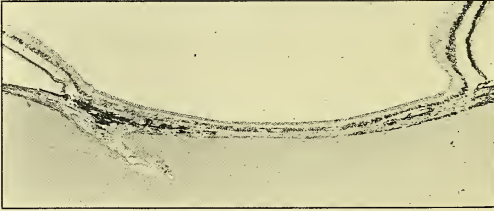


FIG. 448.—CHOROIDO-RETINITIS. $\times 28$.

Adhesion of the retina to the choroid; extreme atrophy of the choroid.

act simultaneously upon the retina. In this manner both retina and choroid may undergo complete atrophy. The relative amount of atrophy in the retina and the choroid may vary within wide limits (*cf. Figs. 448, 449*).

Such cases are much commoner than those to which the term "choroido-retinitis" is generally applied in the narrower sense. These

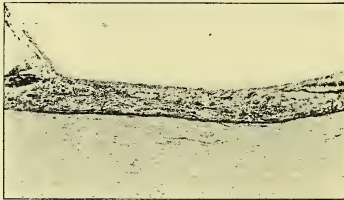


FIG. 449.—CHOROIDO-RETINITIS. $\times 55$.

From a girl, *æt.* 9, with anterior staphyloma. Patch of retino-choroiditis at the macula. Note atrophy of retina. (Contrast with Fig. 448.)

are those which so closely resemble retinitis pigmentosa, except that the clinical history of this disease is wanting, and the distribution of the pigmented patches is not characteristic (*cf. Stein*). In the less advanced stages or foci the appearances exactly simulate disseminated choroiditis, whether they agree with this condition in their syphilitic origin or not. The pigment epithelium is degenerated, heaped up,

partially depigmented, etc., the nervous elements of the outer layers of the retina have disappeared, and are being replaced by fibrous tissue. Later, the patch is adherent to the choroid or closely interwoven with it, the membrane of Bruch having been destroyed. Pigment has invaded the degenerated retina, and forms clumps irregularly scattered but especially aggregated in the perivascular lymph spaces. In flat preparations there is not the regular distribution of pigment which is characteristic of ordinary retinitis pigmentosa; it is densest at and around the affected patches, whilst the intermediate areas may be normal or more commonly deficient in pigment. These intermediate parts of the retina may be detached from the choroid by the accumulation of subretinal fluid, or they too may be adherent, though not interwoven.

OELLER.—A. f. A., viii, 1879. NAGEL.—A. f. A., xxxvi, 1898. HENDERSON.—R. L. O. H. Rep., xv, 1902. STEIN.—A. f. O., lvi, 3, 1903.

RETINITIS PROLIFERANS

The condition now commonly known as retinitis proliferans was first figured in Jäger's 'Ophthalmoscopic Atlas' (1869). This name was given to it by Manz (1876). It is distinguished by dense masses of connective tissue which spread out from the disc or its vicinity, or rarely from other parts of the retina, and come forwards into the vitreous, usually getting an anterior attachment near the ora serrata. New-formed vessels, varying greatly in numbers, enter the masses from the retina, and course over its surface. Many of the cases have started with retinal and vitreous hæmorrhages, due either to injury or some morbid condition, such as Bright's disease, etc.

Cases of retinitis proliferans have been examined microscopically by Manz, Banholzer, Denig, Weeks, Percy Flemming, and Wehrli. Observations similar to these are not uncommon in the pathological laboratory, but are only available for general deductions owing to the lack of ophthalmoscopic details, due to glaucoma, opacities of the media, etc. In Manz's case there was complete funnel-shaped detachment of the retina, with signs of cyclitis and obliteration of the angle of the anterior chamber. On the inner surface of the retina was a delicate membrane composed of imbricated cells attached to the retina posteriorly; it was situated external to the hyaloid membrane. Manz regarded the cells as in part endothelial. The retina was thickened, showing increase of Müller's fibres, especially in the nerve-fibre layer.

Denig found Müller's fibres hypertrophied, the inner nuclear layer distorted, and the nerve-fibre layer atrophied. The new formation consisted of spindle-shaped cells, and was partly in contact with the hyaloid and partly with coagula.

Banholzer examined an eye eight months after injury. The retina was much thickened and ridged; a white band surrounded the disc, whence other bands extended forwards. From one of these a thin membrane stretched into the vitreous. Müller's fibres were hypertrophied, and their inner ends split; there were also new-formed fibres. There were marked signs of cyclitis.

Weeks reports two cases, the second very scantily. In the first the vitreous chamber was almost completely filled with blood, on removing which several membranes were seen. One was attached to the retina near the ora serrata, and formed a loose, almost complete, diaphragm just anterior to the equatorial plane of the globe. Another took origin from near the optic nerve, spread out, and reached the equator. The new-formed membranes were composed partly of young connective-tissue cells, spindle-shaped formative cells, and in the older parts of fully developed connective tissue. The vessels were thickened, the inner layers of the retina showed fibrous degeneration, and the ganglion-cells had disappeared. A fibrous process projected forwards into the

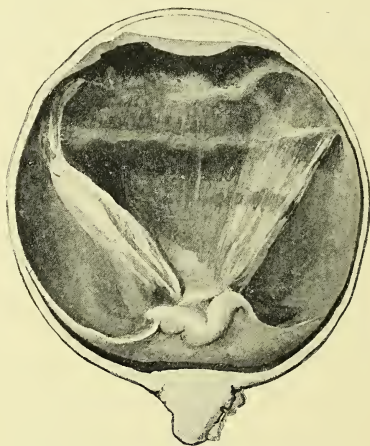


FIG. 450.—RETINITIS PROLIFERANS.

Percy Flemming, T. O. S., xviii. The lower half of the right eye.

vitreous from the optic nerve, made up mainly of prolongations from the connective tissue of the disc. The membrana limitans was apparently absent over this projection and at the neighbouring part of the retina.

Flemming's is the most valuable contribution to the subject. The patient was a man, *æt.* 22, with chronic nephritis. A month before death there was an extensive vitreous hæmorrhage obscuring all details of the fundus; at the site of the disc a white mass projected forwards, and from the upper part of this white bands could be traced peripherally; no vessels could be made out on the bands. *Tn.* On examination, the retina was found to be detached over an area 15.5 mm. in diameter; the middle third of the detached portion was white and folded, 1.8 mm.

in thickness. Laterally, and running from behind forwards, were three sharp ridge-like projections of the retina. The cavity of the eyeball was divided into two compartments, a central funnel-shaped one and a peripheral one, separated by a thin membrane attached posteriorly to the middle of the detached retina for a distance of 3·2 mm., spreading out anteriorly to be attached to the ora serrata, and having its greatest thickness at its posterior attachment. The central cavity contained vitreous; the outer cavity was partly occupied by a large blood-clot, which was in contact with the outer surface of the membrane, extending nearly to the ora serrata, its anterior end having a distinctly serrated appearance. Microscopically the optic disc was much swollen, the



FIG. 451.—RETINITIS PROLIFERANS.

From the same specimen. Section of the retina, showing a hæmorrhage, *c*, in the superficial layers, and blood-corpuscles adhering to the inner surface, *i.e.* anterior to the internal limiting membrane, *m.l.i.*

swelling mainly consisting of spindle-shaped cells with a few round cells. In the thickened folded portion of the retina the rods and cones had disappeared, the outer reticular layer was increased in width, and the fine Müller's fibres seemed more numerous and distinct than usual. The layers internal to the inner nuclear layer were much disorganised; the membrana limitans was absent here. This part gradually merges into more normal retina, the inner limiting membrane reappearing. In places there were hæmorrhages in the nerve-fibre layer, and some sections showed such a hæmorrhage rupturing the interna, a layer of blood-corpuscles adhering to the inner surface of the retina (Fig. 451). Other hæmorrhages were present in the deeper layers, and near the disc were large cyst-like spaces filled with hyaline material. The vessels were not very numerous, and did not show any thickening.

In the region of the ora serrata important changes were observed. At a point corresponding with the attachment of the membrane, Müller's fibres, normally more prominent here, appeared drawn out, elongated, and broken, and gave rise to a triangular projection, the apex being directed inwards. The posterior side of this projection was continuous with the *membrana limitans interna*. Springing from the apex of the projection was the delicate membrane consisting of distinct nucleated fusiform cells, two or three deep. Deeper sections through the same region showed extensive hæmorrhage into the spaces formed by the stretched and broken Müller's fibres, and a direct continuity could be traced between the membrane and the fibrous tissue of the retina. In one section a new blood-vessel with endothelial walls was seen applied



FIG. 452.—RETINITIS PROLIFERANS,

From the same specimen. Section near the ora serrata. *m.l.i.* Membrana limitans interna. *a.* Blood-clot becoming organised. *b.* New membrane attached to the retina.

to the posterior side of the projection, immediately internal to the internal limiting membrane, and entering the base of the membrane. In the angle between the posterior side of the projection and the retina was a large collection of red corpuscles. In some of the sections the corpuscles only were to be distinguished; in others there were numerous large well-stained cells intermingled with them, whilst in others the corpuscles merged into well-defined connective-tissue membranes with large lacunar spaces; in all cases the new membranes were on the side of the clot nearest to the retina. The lacunar spaces were not lined with cells, and did not appear to be blood-vessels.

In some sections at the posterior part (Fig. 453) the membrane, consisting of similar fusiform cells, was seen applied to the retina; in

others there was a tongue-shaped projection forwards, the base of which was clearly continuous with the retinal fibre-layer, and in another such a projection shows at its base either a small hæmorrhage or a new vessel. The appearances suggest that the membrane has contracted, and in doing so has pulled out Müller's fibres on the one hand, and on the other has dragged the retina away from the choroid.

Flemming thinks that the membrane, from its attachments, must be related in some way to the hyaloid, but its definite structure shows that it is something more than the hyaloid. From the character of the cells composing it, from its relation to the blood-clot at its anterior attachment, and its connection with the retina posteriorly, he regards it as a new formation. Repeated hæmorrhages are a feature in the clinical records of cases of retinitis proliferans, and in this case—a patient

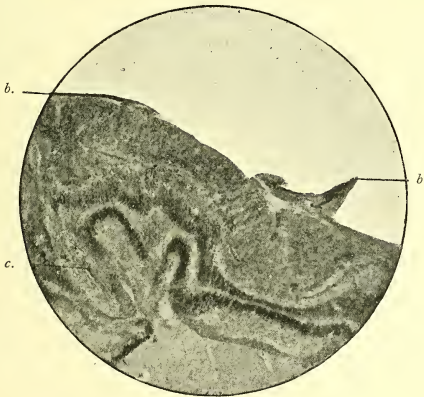


FIG. 453.—RETINITIS PROLIFERANS.

From the same specimen. Section through the retina posteriorly. *b.* New membrane. *c.* Thickened and folded retina.

suffering from Bright's disease—such recurrences are very likely. Flemming thinks that a retinal hæmorrhage occurred, which ruptured the interna and spread itself out as a thin layer between this and the hyaloid. Owing to the inflammatory process present at the time in the retina and papilla—there was well marked neuroretinitis in the other eye—the clot became organised, *i.e.* new tissue elements derived from the retina grew into the clot. This new tissue would be more or less completely incorporated with the hyaloid, but anteriorly near the ora serrata a separation exists for a short distance. In this way the hyaloid would become thickened and strengthened. If at this stage another and more extensive hæmorrhage took place, it might strip up the thickened hyaloid and give rise to the appearances shown in the

specimen. It would be difficult to imagine such an extensive hæmorrhage being resisted by a normal hyaloid.

Many clinical cases of retinitis proliferans have been recorded, and the opinions expressed by the authors require consideration. Most of them regard retinal or vitreous hæmorrhages as the essential factor (Manz, Leber, Pröbsting, Schleich, Banholzer). Pröbsting succeeded in producing a certain amount of retinal proliferation by the experimental injection of blood into the vitreous of rabbits. Schultze considers the membranes to arise from simple deposits of unabsorbed fibrin. Denig thinks that the reabsorption of blood-clot is prevented by coincident disease of the blood-vessels. Other authors deny the necessity of hæmorrhage, and attribute the condition to a localised proliferation of Müller's fibres.

Mackenzie described a case which probably belongs to this category, in which there was oxaluria. Several cases occurred during the course of Bright's disease (Pröbsting, Martinet, Flemming, Wehrli). In almost all there was some cause of local or general circulatory disturbance, such as heart disease, diabetes, arteriosclerosis, etc.

Flemming considers that there must be some factor other than mere hæmorrhage to explain why it is that the clot in these particular cases becomes organised, and why an excess of fibrous tissue is found in the retina. This second factor must be of the nature of an inflammatory process, such as has been described under the name "plastic retinitis," affecting mainly the sustentacular tissue of the retina. The sclerosis, here as in the nervous system, where neuroglia is similarly involved, is probably due to some toxic agent, or possibly several. The frequency with which retinitis proliferans occurs in both eyes points to some general cause being present, though this may merely act in the way of producing hæmorrhage.

From my experiments on the healing of retinal wounds (*v. p.* 547) I have found reason to doubt the preponderant importance of the neuroglia in the production of fibrous tissue in and about the retina. I think the sequence in retinitis proliferans is probably as follows: Some toxic condition leads to a retinal hæmorrhage. If it is situated in the peripheral parts of the retina, or is due to rupture of the smaller vessels nearer the papilla—in other words, if it is a small hæmorrhage—no large proliferation of new tissue will result. A scar will follow the organisation of the clot through the medium of the scanty mesoblastic tissue of the smaller retinal vessels. If, however, a large hæmorrhage occurs, it will be in the neighbourhood of the disc, or if caused by repeated hæmorrhages in slightly more peripheral parts, will yet invade the neighbourhood of the larger vessels, *i. e.* again the neighbourhood of the disc. Now it is around the larger vessels, and *par excellence* upon the disc, that the main mass of retinal mesoblastic tissue is situated. At the papilla itself we have not only the walls of the vessels, but also remnants of the hyaloid artery and a ring of anastomoses with posterior ciliary vessels—in fact, the largest mass of mesoblastic tissue found in the walls of the true optic cup. The nearer the hæmorrhage approaches this point, and the more widespread its traumatic and irritating effects in this immediate neighbourhood, the more tissue

will be excited to reparative reaction, and the greater will be the proliferation and organisation. Hence the fact that retinitis proliferans invariably springs from the disc or its vicinity. In the periphery there are two factors acting against such proliferation—first, the smallness of the hæmorrhage, which, however, may possibly be increased by repetition or multiplicity and confluence; secondly, and more important, the small amount of tissue which is capable of proliferating and inducing organisation. Upon this hypothesis the toxic agent acts only, or at any rate chiefly, by producing retinal hæmorrhage, and only secondarily, or not at all, by producing an inflammatory process in the retina and papilla. Against the latter hypothesis are the facts that the relatively healthy retina may show no marked signs of any such inflammatory process being present, and that the toxic conditions so frequently present, whilst potent causes of hæmorrhage and even of inflammatory conditions, are, with the possible exception of nephritis, not known to be specially effective in leading to fibrous tissue proliferation.

Since arriving at these conclusions I find that Wehrli and Römer had already noticed that the new fibrous tissue in their cases sprang from the proliferated adventitial tissue of the central retinal vessels. They, however, consider that the neuroglia also proliferates—a point which I consider not proven, though not improbable. Römer thinks that retinitis proliferans is not always due anatomically to a single cause, and that the opinions of previous observers may all be true.

JÄGER.—*Ophthalmoscop. Handatlas*, 1869. MANZ.—*A. f. O.*, xxii, iii, 1876; xxvi, 2, 1880. BANHOLZER.—*A. f. A.*, xxv, 1892. DENIG.—*A. f. A.*, xxx, 1895. WEEKS.—*T. Am. O. S.*, 1897. *FLEMMING.—*T. O. S.*, xviii, 1898. WEHRLLI.—*A. f. A.*, xxxvii, 1898. LEBER.—*In G.-S.*, v, 1877. PRÖBSTING.—*K. M. f. A.*, xxviii, 1890. SCHLEICH.—*K. M. f. A.*, xxviii, 1890. SCHULTZE.—*A. f. A.*, xxv, 1892. MACKENZIE.—*Ann. d'Oc.*, liii, 1865. MARTINET.—*Deutsch. med. Woch.*, 1891. SCHOLZ.—*Ungar. Beiträge zur Augenheilkunde*, ii, 1900. PARSONS.—*R. L. O. H. Rep.*, xv, 3, 1903. RÖMER.—*A. f. O.*, lii, 3, 1901. MARPLE.—*T. Am. O. S.*, 1901. CIRINCIONE.—*Hirschberg's Festschrift*, 1905; *La Clinica oculistica*, 1905.

SYPHILIS

Early stages of syphilitic retinitis have not been examined microscopically, and nearly all the later stages which have been investigated have had choroidal changes which were probably primary. Hence the appearances are those which have already been described (*see* "Choroiditis disseminata," "Choroido-retinitis," etc.). Bach's case forms an exception; it was observed ophthalmoscopically, and showed diffuse retinitis for about six papilla diameters around the disc, with vitreous opacities. The changes were confined to the retinal vessels, the choroidal ones being quite free from inflammation.

Hutchinson and Bader (1858) made the first histological examination, and this was followed by Edmunds and Brailey (1880). The latter found thickening of the walls of the vessels, and infiltration around them; there was no sign of proliferation. Nettleship (1886) noted increase in the nuclei in the walls of the smaller vessels; the adventitia of the arteries was thickened, sometimes hyaline; the muscular coat was

scarcely recognisable, so that arteries could only be distinguished from veins by their greater thickness; there were groups of cells with deeply

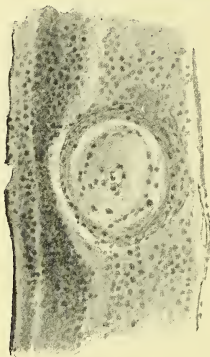


FIG. 454.—VASCULAR CHANGES IN SYPHILIS.

Holmes Spicer, T. O. S., xii. From a case of congenital syphilis. Transverse section of a retinal vessel, showing endothelial thickening of the intima and some thickening of the adventitia. The lumen is still present.



FIG. 455.—VASCULAR CHANGES IN SYPHILIS.

From the same specimen. Longitudinal section.

stained nuclei in the adventitia and around the vessels. In some vessels, probably veins, only the inner layers were thickened.

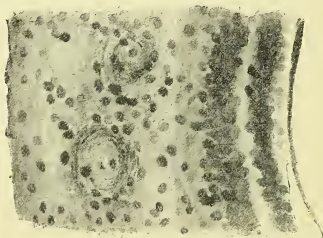


FIG. 456.—VASCULAR CHANGES IN SYPHILIS.

From the same specimen. Sections of a retinal artery (above) and vein (below). Both are thickened, but the vein has a deposit of almost structureless fibrous tissue in the inner coat.

Holmes Spicer described similar changes (Figs. 454-6). Uhthoff found infiltration of the adventitia of the veins as well as of the arteries, and the aggregation of cells was sometimes so great that the lumen

was invisible. Appel described annular and partial endo- and periarteritis, slight infiltration of the adventitia in the veins, and obliteration of many of the capillaries. Baas noted that where the vessels had pigment around them these were most sclerosed. The obliteration of some of the vessels leads to dilatation of the others in the same area. It will be noticed that the changes which have been described have been most marked in the vessels, and are not pathognomonic.

Gummatous infiltration of the retina has been described by Brixia in a case of bilateral gumma of the ciliary body. The changes resembled those which I have described in similar cases, and consist essentially in œdema, infiltration, and necrosis. They show no characteristic features.

HUTCHINSON AND BADER.—R. L. O. H. Rep., i, 1858; ii, 1860. EDMUNDS AND BRAILEY.—R. L. O. H. Rep., x, 1880. NETTLESHIP.—R. L. O. H. Rep., xi, 1886. HOLMES SPICER.—T. O. S., xii, 1892. UHTHOFF.—A. f. O., xxxix, 1893. APPEL.—Dissert., Würzburg, 1894. BACH.—A. f. A., xxviii, 1894. ROCHON-DUVIGNEAUD.—A. d'O., xv, 1895. NAGEL.—A. f. A., xxxvi, 1898. BAAS.—A. f. O., xlv, 3, 1898. BRIXIA.—A. f. O., xlviii, 1, 1899. PARSONS.—T. O. S., xxii, 1902; R. L. O. H. Rep., xv, 1903.

TUBERCLE

In nearly all cases tubercle of the retina is secondary to affection of the uveal tract or optic nerve. The deposits are found most commonly in the nerve-fibre layer, and have the usual structure, consisting of epithelioid cells, and granulation tissue, derived from the vessels, lymphoid cells, and giant cells, the two latter being often scanty. Necrotic changes may be present, and may even involve the whole retina. Cases of tubercle of the retina, in which other parts have also been affected, have been reported by Démours, Cruveilhier, Sattler, Weiss, Wagenmann, Schöbl, Bongartz, Dobson, Portland, Bach, de Lieto Vollaro, Lubowski, Dorls, Litten, A. Knapp, and others (*see also* "Tubercle of the Optic Nerve").

The best authenticated case of primary tubercle of the retina is that of O'Sullivan and Story. The patient was a healthy girl, æt. 21. There was a history of sudden failure of sight in the right eye three months previously. Ophthalmoscopically there was the appearance of intense papillitis, differing, however, from the ordinary picture in the brilliant whiteness and extreme swelling, with large tortuous vessels. There were white spots at the macula. The eye was removed two months later. In the posterior part of the retina there was a tumour, $\frac{1}{8}$ inch in diameter, at and around the disc. The retina was detached on each side, the space between it and the choroid being occupied by a homogeneous coagulum. The choroid, covered with intact pigment epithelium, was quite normal. Microscopically the tumour consisted of typical tubercle systems, composed of small round cells, large irregular cells, and giant cells. Parts were caseated and traversed by strands of connective tissue containing blood-vessels. Situated in the internal layer of the retina in the immediate vicinity of the large mass were numerous scattered nodules, consisting of lymphoid and endothelial cells in a reticulum. The retinal pigment epithelium, choroid, and optic nerve were normal. Eighteen months later the patient was in

good health ; an uncle died of meningitis, and a maternal relative died of consumption. No mention is made of tubercle bacilli.



FIG. 457.—TUBERCLE OF THE RETINA.

Hancock, R. L. O. H. Rep., xvi. Showing the folding of the retina, and the anterior and posterior plaques separated from one another by easily traceable retinal layers.

The next most important case has recently been published by Hancock. A healthy man, *æt.* 19, complained of failure of sight in the

right eye of about eight months' duration: the personal and family histories were negative. Ophthalmoscopically there was a large yellowish-white area to the outer side of the disc, extending over the macular region; it was raised about 1·5 mm.

Macroscopically the vitreous, which was quite clear, was found to be abnormally adherent to the surface of the patch, tearing away from it with difficulty. The retina remained *in situ*, but on subsequently passing the eye through spirit it became detached, and it was at once seen that the morbid focus was entirely confined to the retina, the choroid and overlying pigment epithelial layer both to the naked eye and examination with the corneal loupe appearing quite normal.

Microscopically the retina was thrown into numerous folds and



FIG. 458.—TUBERCLE OF THE RETINA.

Hancock, R. L. O. H. Rep., xvi. Showing the anterior and posterior plaques connected by a fibrous strand which perforates the intervening retinal layers.

separated from the choroid by a narrow band of exudation, staining deeply with eosin (Fig. 457). The choroid was normal in appearance, the membrane of Bruch intact and covered by an apparently unaltered layer of hexagonal pigment epithelium. In the thickened folded retina were two well-defined plaques of granulation tissue; these in the majority of the sections were seen to be quite distinctly separated from one another by retinal layers, which, though quite recognisable, had undergone more or less change; but in a few sections they were seen to be connected by a band of fibrous tissue which, as it were, perforated the intervening retinal layers (Fig. 458). The anterior or internal plaque, confined to the nerve-fibre layer, was chiefly composed of ill-developed fibrous tissue containing well-marked giant cells, and exhibited

extensive round-celled infiltration (Fig. 459). The giant cells were of the large branching type, with well-defined nuclei arranged without exception in the centre of the cell. The small-celled infiltration was especially evident in the perivascular lymph spaces and bore no definite relation to the giant cells, nor were the latter surrounded by any epithelioid cells as in typical tubercular systems.

The posterior or external plaque, confined to the rod and cone and external nuclear layer, was also chiefly made up of cellular fibrous tissue, but differed markedly from the anterior in containing a large number of blood-vessels and proliferated pigment epithelium, and there was an entire absence of giant cells. The whole affected area was sharply limited, passing abruptly into œdematous but otherwise normal retinal tissue. No tubercle bacilli could be demonstrated. Whether



FIG. 459.—TUBERCLE OF THE RETINA.

Hancock, R. L. O. H. Rep., xvi. The anterior plaque under a high power, showing giant cells and small-celled infiltration.

the anterior or the posterior plaque was the primary seat of the lesion it seemed impossible to determine. The cornea, iris, lens, ciliary body, and optic nerve were normal.

L. Müller has described retinal changes resembling miliary tuberculosis in a case of miliary actinomycosis.

DÉMOURS.—*Traité des Maladies des Yeux*, i, 1818. CRUVEILIER.—*Traité d'Anat. path. gén.*, iv. SÄTTLER.—*B. d. o. G.*, 1877; *A. f. O.*, xxiv, 3, 1878. WEISS.—*A. f. O.*, xxiii, 4, 1877. WAGENMANN.—*A. f. O.*, xxxiv, 4, 1888. SCHÖBL.—*C. f. A.*, xii, 1888. BONGARTZ.—*Dissertation*, Würzburg, 1891. DOBSON.—*Lancet*, 1892. PORTLAND.—*Ann. d'Oc.*, xli, 1859. BACH.—*A. f. A.*, xxviii, 1894. DE LIETO VOLLARO.—*Arbeiten aus d. Augenlinik zu Neapel*, v. LUBOWSKI.—*A. f. A.*, xxxv, 1897. DORLS.—*Ueber einen Fall von Tuberculose der Ader- und Netzhaut*, Würzburg, 1901. LITTEN.—*Deutsche med. Woch.*, 1902. A. KNAPP.—*A. of O.*, xxxii, 1903. EMANUEL.—*K. M. f. A.*, xi, 1902. *O'SULLIVAN

AND STORY.—Trans. Royal Acad. of Med. of Ireland, xvii, 1899. *HANCOCK.—R. L. O. H. Rep., xvi, 2, 1905. L. MÜLLER.—K. M. f. A., xli, 1903. *COATS.—R. L. O. H. Rep., xvi, 1905.

LEPROSY

The changes in the retina in leprosy are slight, if present at all. Bull and Hansen figure small nodules in the anterior parts. Lie found changes only over choroidal nodules, and in a mass of exudate on the surface near the ciliary body. In the former case the retina was infiltrated, and there were occasionally a few bacilli found, but this was rare. Franke and Delbanco, however, found very extensive inflammatory changes, with much thickening, and many clumps of bacilli in both eyes in one case.

BULL AND HANSEN.—The Leprous Diseases of the Eye, London, 1873. JEANSELME AND MORAX.—Ann. d'Oc., cxx, 1898. *BORTHEN AND LIE.—Die Lepra des Auges, Leipzig, 1899. FRANKE AND DELBANCO.—A. f. O., l, 2, 1900.

CYSTS

Mention has already been made of cystic spaces formed in the retina as the result of œdema (*v. p.* 569) and degeneration (*v. p.* 582). Certain forms are worthy of more detailed consideration.

Peripheral Cystic Degeneration.—Rows of small cysts are often found in the retina immediately behind the ora serrata, especially in



FIG. 460.—CYSTS NEAR THE ORA SERRATA. $\times 55$.

From a man, æt. 37; eye removed for corneal ulcer. Iwanoff's cysts.

old age, when they are almost constant, but not infrequently under pathological conditions in other cases (Fig. 460). They were first described by Blessig (1855), subsequently by Henle (1866), and more minutely by Iwanoff (1869). The latter found them in children and adults, but most frequently from 50 to 80 years of age. The oval or round cystic spaces, which he called "colloid cysts," occurred in the inner and outer nuclear layers: they were bounded by the supporting fibres of the retina—Müller's fibres, and the walls were often so attenuated that they communicated with one another. They were usually 2 to 8 mm. behind the ora serrata, and contained an albuminous serum or a gelatinous substance. Iwanoff regarded them as due to an œdema of the retina, and he mentions the coexistence of vascular changes and fatty and calcareous degeneration, attributing special importance to calcareous degeneration of the capillaries. The spaces are at first small and irregular, starting in the outer nuclear layer. Similar spaces appear

in the inner nuclear layer, the outer reticular layer remaining for a time as a thin septum, which later disappears. The true retinal layers gradually atrophy, Müller's fibres become much elongated by stretching (Hulke), and actual growth (Nettleship), so that finally the retina consists merely of these hypertrophied pillars, the ends of which spread out on the outer and inner limiting membranes.

Merkel (1870) found the cysts chiefly in the outer nuclear layer, less frequently in the inner: he noticed the condition in man and in dogs, and regarded it as a senile phenomenon.

Nettleship (1873) found similar cysts in staphylomatous eyes. He regarded the signs of past inflammation of the sclerotic and choroid as important factors in their production. In two specimens there was no detachment of the retina, but thinning and uniform outward bulging of the choroid and sclerotic. The outer surface of the retina followed the altered curve, whilst the inner surface retained its normal situation, so that the two surfaces were widely separated from each other, being connected by drawn-out Müller's fibres. In the third case the sequence was probably: (1) adhesion of the outer surface of the retina to a small patch of choroid by inflammatory adhesion; (2) detachment and more or less shrinking of the retina surrounding the adherent patch; (3) separation of the inner from the outer layers of the adherent part of the retina, with overgrowth of Müller's fibres; (4) owing to the continued retraction of the surrounding detached retina, the part which by its outer layers remained adherent to the choroid became at last separated from that structure and formed the outer wall of the cyst-like patch in the retina. This explanation is probably true in these cases and in other similar ones, but it does not apply to the majority of cases of peripheral cystic degeneration in which there is neither choroiditis nor staphyloma.

Landsberg (1877) attributed the condition to atrophy of the nervous elements; minute cystic spaces are thus formed, which subsequently run together by breaking down of the intervening walls.

According to Kuhnt (1881), the cysts may form in the reticular, ganglion cell, and nerve-fibre layers as well as in the usual situations. He considers that there is always a preliminary degeneration of the retina, involving destruction of the nervous elements and gliosis, for cysts never form in the intact tissues; the minute cysts run together, as suggested by Landsberg, and the transudation from the capillaries is increased, owing to pathological conditions, amongst which atrophy of collateral areas may be a factor. In old people slight inflammatory changes are often present at the ora serrata, leading to adhesion of the retina and choroid; gliosis follows, accompanied by the development of cysts (*v. p.* 582).

Peripheral cystic degeneration is common, and can, therefore, be easily studied. In flat preparations the cysts appear as bright bands, contorted and frequently communicating with each other. The area affected is irregular, having a zigzag outline which does not run parallel to the ora. The retina is thickened, and may be five or six times the normal thickness. In transverse sections the cysts affect the inner nuclear layer and the inner part of the outer nuclear layer—*i. e.* Henle's fibre layer. In this stage they form two parallel rows, separated by the

remnants of the internuclear layer, but the latter are soon broken through, so that a single row of larger cysts results. The walls, formed of drawn-out Müller's fibres, show well-marked oval nuclei, which may be flattened by compression.

The contents of the cysts vary. Generally nothing is seen in ordinary sections, the fluid having been washed out in the course of preparation. Sometimes it is more albuminous, and clings to the walls, so that a homogeneous or granular coagulum is seen, usually shrunk away from the walls. It is only in the presence of simultaneous inflammatory processes that a fibrinous coagulum is found.

BLESSIG.—Dissertation, Dorpat, 1852. HENLE.—Handbuch der syst. Anat. des Menschen, ii, 1866. IWANOFF.—A. f. O., xv, 2, 1869. MERKEL.—Ueber d. Macula lutea d. Menschen u. d. Ora serrata eines Wirbelthieres, Leipzig, 1870. NETTLESHIP.—R. L. O. H. Rep., vii, 1873. LANDSBERG.—A. f. O., xxiii, 1, 1877. KUHN.—K. M. f. A., xix, 1881, Beilageheft.

Cysts in detached retinae.—Cysts are not uncommon in old detached retinae, and may be numerous. O. Becker (1874) gives plates showing the condition. Lawford (1887) found 4 cases in 600 consecutive eyes examined at Moorfields—probably too low a proportion.



FIG. 461.—CYSTS OF THE RETINA.
After Lawson.



FIG. 462.—CYSTS OF THE RETINA.
After Lawson. The retina is turned forwards to show the cysts, which are on the outer side.

In every case the bulging took place outwards, the inner layers of the retina retaining their normal position. The outer wall springs abruptly from the base, which is usually the narrowest part of the cyst. The cysts appear to begin by the formation of spaces in the inner nuclear layer between Müller's fibres. The intact inner layers ultimately degenerate into a nucleated fibrous wall, a process which occurs very early in the outer wall. In one case the separation of layers apparently commenced in the outer reticular layer, or possibly in the inner half of the outer nuclear layer, in no case in the outer nuclear layer. Vernon described an eye the retina of which contained 11 small cysts.

Treacher Collins found 9 cases in two years at Moorfields, probably about double the frequency cited by Lawford. In two the spaces were between the two nuclear layers; in the others the retina was too degenerated to determine the exact site. This author regards the condition as dependent upon lymph stasis occurring in connection with detached retina. He also records a case of Tweedy's which was observed clinically as well as anatomically. Clinical observations of

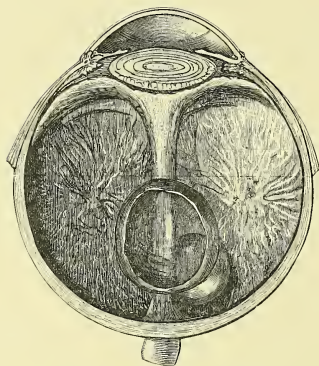


FIG. 463.—CYSTS OF THE RETINA.

R. L. O. H. Museum. Showing cysts protruding from the outer surface of the detached retina.



FIG. 464.—CYST OF THE RETINA. $\times 7$.

From the same specimen as Fig. 223, vol. i. Note degenerated ciliary body above to left, and cataractous lens above to right. The cyst projects upon the outer and posterior surface of the detached retina; it is filled with coagulated exudate.

retinal cysts have been made by Merkel in the dog and Eversbusch in an old horse and a calf. Cysts have not infrequently been diagnosed from ophthalmoscopic appearances (*cf.* Darier, Marcus Gunn).

Falchi described an eye with numerous cysts in a detached retina following plastic iridocyclitis and secondary glaucoma. The cysts were at the equator and posterior pole, and contained fibrinous and fibrinous-hæmorrhagic coagula, which lay in masses of thickened neuroglia. Similar smaller cysts had developed in the walls of the larger ones. Falchi lays stress on the association of retinal cysts with angiosclerosis, the more diseased parts of the vessels being surrounded by exudates which lead to the formation of cysts, and also cause detachment of the retina.

Like most of the cysts reported above, probably the majority of



FIG. 465.—CYSTS IN DETACHED RETINA. $\times 8\frac{1}{2}$.

From a child, æt. $1\frac{3}{4}$; globe shrinking after perforating wound. Formation of cysts by adhesion of folds of detached retina; part of a large cyst is seen on the right below.

those found in detached retinæ commence in the degenerated membrane. Others are due to adhesion of folds of the retina. Many originate between new-formed fibrous membranes, usually on the inner surface of the retina and the retina itself; these often contain blood in a more or less altered condition. These are not true cysts of the retina, but are indistinguishable from them in many cases.

BECKER.—Atlas der path. Topographie des Auges. LAWFORD.—R. L. O. H. Rep., xi, 1887. VERNON.—Trans. Path. Soc., xix. WEBSTER.—New York Med. J., 1887. KAMOCKI.—A. f. A., xvii, 1887. TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1893. DARIER.—A. d'O., x, 1890. GUNN.—T. O. S., x, 1890. PANAS AND RÉMY.—Anat. path. de l'Œil, Paris, 1879. EVERSBUSCH.—Z. f. vergleich. Augenheilkunde, iv, 1887. GREEFF.—A. f. A., xxv, 1892. FALCHI.—A. f. O., xli, 4, 1895.

TUMOURS.

GLIOMA.

The first case of glioma on record was published by Hayes (1767) : Wardrop (1809) gave the first precise clinical, and Robin (1854) the first accurate histological description. The subject received the attention of Virchow in 1864, and in 1868 Hirschberg published a paper which was followed by a monograph in the next year. Glioma was included in Knapp's treatise on intra-ocular tumours at about the same period, and was also studied by Iwanoff. Another book on tumours was published by da Gama Pinto in 1886, and in recent times glioma has been treated exhaustively in an excellent monograph by Wintersteiner (1897), and in Lagrange's treatise on 'Tumours of the Eye' (1901). The literature on the subject is very vast, and will be referred to as far as is compatible with the limits of space in the detailed description. Amongst the papers of special importance those of Lawford and Treacher Collins, and of Devereux Marshall may be mentioned.

HAYES.—*Med. Observations and Inquiries*, iii, 1767. WARDROP.—*Observations on Fungus hæmatodes*, Edinburgh, 1809. ROBIN.—*Gaz. méd. de Paris*, 1854. VIRCHOW.—*Onkologie*, ii, 1864. HIRSCHBERG.—*A. f. O.*, xiv, 2, 1868; *Der Markschwamm der Netzhaut*, Berlin, 1869; *C. f. A.*, xxviii, 1904. KNAPP.—*Die intraocularen Geschwülste*, Karlsruhe, 1868. IWANOFF.—*A. f. O.*, xv, 2, 1869; *Jl. de l'Anat. et de la Phys.*, vii, 3, 1870. DE GAMA PINTO.—*Untersuchungen ü. intraoc. Tumoren*, Wiesbaden, 1886. *LAWFORD AND TREACHER COLLINS.—*R. L. O. H. Rep.*, xiii, 1, 1890. *DEVEREUX MARSHALL.—*R. L. O. H. Rep.*, xiv, 3, 1897. *WINTERSTEINER.—*Das Neuroëpithelioma retinae*, Leipzig u. Wien, 1897. *LAGRANGE.—*Tumeurs de l'Œil*, i, Paris, 1901. *OWEN.—*R. L. O. H. Rep.*, xvi, 1905.

Glioma retinae forms about 0·04 per cent. of all diseases of the eye (Wintersteiner). It occurs exclusively in children; in two thirds of the cases (314 out of 467) it was noticed before the end of the third year; many (34)—probably all—are congenital. In 429 cases, 221 were male and 208 female. In 405 cases, 308 were unilateral (143 right, 165 left), 97 bilateral (37 right first, 49 left first). In Lawford & Collins's 60 cases, 43 were unilateral (16 right, 27 left), 12 bilateral; in Marshall's 32 cases, 19 were unilateral (10 right, 9 left), 12 bilateral. In bilateral cases both eyes may be affected at birth (Helfreich, Snell); more frequently disease in the second eye is noticed months or even years after the first—3 years (Treacher Collins), 2½ years (Lawford). In any case the growth in the second eye is an independent focus. Several members of the same family may be affected (Lerche, Sichel, v. Graefe, Wilson, Newton, Calderini, Fuchs, Marshall, Snell, etc.); in Wilson's cases 8 children of a family all had glioma; in Newton's 10 out of a family of 16 had glioma, 7 being bilateral; of the 10 none lived beyond the age of 3, except one, who died of recurrence at the age of 5; 5 were males, 5 females. There is one doubtful case on record of a child from whom a gliomatous eye has been removed growing up and having children with glioma (Owen). Lawford and Collins report several cases in which relations had tumours of various kinds.

Glioma retinae runs through the same stages as other intra-ocular tumours, viz., (1) intra-ocular growth; (2) secondary glaucoma; (3) extra-ocular extension; (4) metastasis. The glaucomatous stage may arise suddenly, *e. g.* after an injury or instillation of atropin (Hirschberg). It results in enlargement of the globe, followed by apparent or real exophthalmos. Stretching of the walls of the eye may manifest itself first as megalocornea (Vetsch) or keratomegaly (Parent) (*v. p.* 641). Later, the sclerotic stretches, usually in the intercalary zone, in other cases between the insertions of the recti and the equator, seldom at the posterior pole. In the last two groups there is proptosis, which is much increased in the third stage, if the extra-ocular extension is retrobulbar. The third stage is usually accompanied by great diminution of pain, owing to relief of tension. There is generally a discharge of yellow material, which may be pus if severe keratitis has supervened. Perforation often occurs at the limbus, and is followed rapidly by fungating growth. The lids are seldom infiltrated, but are stretched and thinned. Metastasis first occurs in the preauricular and neighbouring glands, later in the cranial and other bones (ribs, humerus, etc.). Direct extension by continuity to the optic nerve and brain, cranial bones, etc., is commoner; and metastases in other organs (usually the liver) are relatively uncommon (*cf.* Sarcoma). In most cases the first stage lasts from six months to a year; statistics of the second stage are few and untrustworthy, and vary from a few weeks to twenty-one months (mean, seven months).

HELFFREICH.—*A. f. O.*, xxi, 2, 1875. SNELL.—*T. O. S.*, iv, 1884. TREACHER COLLINS, LAWFORD.—*T. O. S.*, xvi, 1896. WILSON.—*Brit. Med. J.*, 1872. NEWTON.—*Lancet*, 1902. HOSCH.—*A. f. A.*, xviii, 1888. FUCHS.—*Lehrbuch*. SNELL.—*T. O. S.*, xxiv, 1904. JESSOP.—*St. Bartholomew's Hosp. Rep.*, xxxviii, xxxix. PARSONS.—*Clinical J.*, xxv, 1905. OWEN.—*R. L. O. H. Rep.*, xvi, 1905.

Macroscopic appearances and general structure.—*Glioma*, before hardening, is a soft, almost fluid, tumour, of milky whiteness, showing on section red spots and lines where the blood-vessels are cut across, and sometimes hæmorrhages. In other cases the growth is grey or yellow, with chalky white spots, or occasionally gelatinous and semi-transparent. It resembles nearly brain tissue, hence the name “medullary cancer” (Markschwamm, Hirschberg). The white spots are gritty, and are due to calcareous degeneration (Robin). Old hæmorrhages may be represented by pigmentation.

In the early stages there are usually several nodules (rarely only one), the larger ones being surrounded by smaller satellites. The main mass of the growth is usually in the subretinal space, on the outer side of the retina, which is detached (*Glioma exophytum*, Hirschberg) (Fig. 466). Much less frequently the retina is *in situ*, or only slightly raised from the choroid; the growth is not flat on the inner surface, as in the usual type, but irregular, with polypous outgrowths (*Glioma endophytum*, Iwanoff, Hirschberg) (Fig. 467); in this case the retina is more generally affected and uniformly thickened. The distinction is of some clinical, but of little pathological importance.

Glioma in stained sections shows a quite characteristic appearance even with very low magnification. The stain is strongly taken up in



FIG. 466.—GLIOMA EXOPHYTUM. $\times 3$.
Note the invasion of the anterior part of the optic nerve.

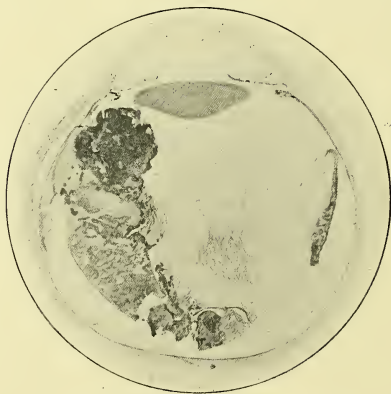


FIG. 467.—GLIOMA ENDOPHYTUM. $\times 2\frac{1}{2}$.
From a girl, æt. 6. The growth invades the vitreous and has many hæmorrhages; there is a large hæmorrhage anteriorly, shown by the dark area.

convoluted lines and dots, separated by masses which only take up the protoplasmic stains. With a higher power, the deeply stained parts are seen to consist of circles and cylinders of thickly grouped cells, arranged in 10-20 layers around and along axial blood-vessels. Between these perivascular sheaths are necrotic or fattily degenerated cells, which only stain diffusely or not at all with nuclear stains. The arrangement is particularly well seen in sections stained with hæmatoxylin and eosin: here the blood-corpuscles which are usually packed in the vessels stain deeply with eosin, and form a centre surrounded by a ring of deep blue nuclei, outside which are irregular necrotic areas which stain red, with or without a transition zone of purple.

This peculiar structure was made out first by Iwanoff, and led



FIG. 468.—GLIOMA RETINÆ. $\times 55$.

From a girl, æt. 6, showing the mantle of cells around the vessels.

da Gamo Pinto to describe the tumours as *glio-angiosarcoma* or tubular glio-sarcoma. It is invariably present in the early stages (Flexner, Jung, Wintersteiner), in spite of which it has often been described as a rare occurrence (Eisenlohr, van Duyse, etc.). The intermediate zone, when present, is a fourth to a third as thick as the nuclear ring. The cause of the structure is the progress of the growth in the immediate vicinity of the newly forming blood-vessels, as is shown by the rich supply of mitoses here (Mazza), and by dahlia-fuchsin staining, whereby the younger cells are stained red and the older blue (Eisenlohr). The necrotic areas are due to insufficient nourishment of the rapidly growing cells at a short distance from the vessels, and this explains the transition zone. This is often absent, however, the line of demarcation being so sharp that one suspects the presence of a membrane: there is never one, but often a cleft in hardened sections.

Wintersteiner explains this condition as follows: the tumour cells are dependent upon the vessels for nourishment; as the latter grow they draw their cellular mantle after them, pushing the neighbouring tissues apart, whereby it often happens that they come into immediate contact with necrotic areas. Both views account for the fact that the cellular coils are often apposed to calcareous deposits, which are common in the dead parts.

The first sign of cell degeneration is seen in the nuclei being



FIG. 469.—GLIOMA RETINÆ.

From a photograph by Lister. Showing a typical blood-vessel surrounded by a mantle of cells, the nuclei of which stain deeply with hæmatoxylin. Outside this mantle are necrotic, badly staining cells.

smaller and more deeply stained, and later the deeply staining zone is narrowed.

FLEXNER.—*Johns Hopkins Hospital Bulletin*, 1891. JUNG.—*A. f. O.*, xxxvii, 4, 1891. EISENLOHR.—*Virchow's Archiv*, cxxiii, 1891. VAN DUYSE.—*A. d'O.*, xiv, 1894. MAZZA.—*Ann. di Ott.*, xvii, 1888.

The cells.—The main mass of cells are small, with large nuclei. These are round or oval, 6–7 μ in diameter, coarsely granular, with a single small nucleolus. The cytoplasm is extraordinarily sparse, so that the nuclei have often been described as free (Virchow). The cells are 8–9 μ in diameter, but may be 12 μ where rapid proliferation is going on; the latter are commonest in extra-ocular tumours (Virchow) and cerebral metastases (Noyes), a fact which led to the diagnosis of transition forms to sarcoma (gliosarcoma).

The cells are round when the cytoplasm forms a thick sheath; irregular, with short, pointed processes, when more developed. Treacher Collins has pointed out the resemblance of these to the embryonic cells found in the retina (*vide infra*). Other cells, with

granular protoplasm and one or more long processes, also occur, resembling amœboid cells (Vetsch).

Virchow first regarded the cells as products of the neuroglia, and instituted the term "*glioma retinæ*." This opinion was opposed by Delafield, who called the growths small round-celled sarcomata.

Besides the small polymorphic cells there are several other types :

(1) *Cylindrical cells*.—These are only the better nourished small cells, as shown by the position in which they are found, viz. in the layer juxtaposed to the vessel wall (though these are not invariably cylindrical), on the surface of the choroid, on the surface of the iris. Mazza called these sarcomatous, a view which involves the very improbable transition of sarcoma cells into glioma cells.

(2) *Spindle-shaped cells*.—These are due to growth in narrow clefts,

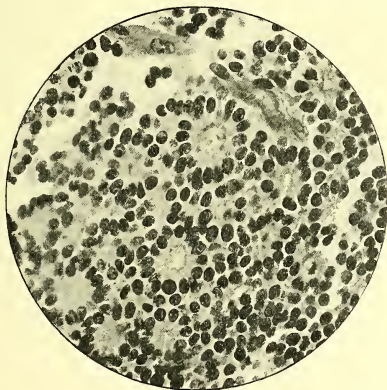


FIG. 470.—GLIOMA RETINÆ.

From a photograph by Lister. Showing neuro-epithelial rosettes.

e. g. between the lamellæ of the cornea, and exceptionally in the choroid and optic nerve.

(3) *Rosettes*.—These were discovered by Flexner, who instituted the term "*neuro-epithelioma*," which has been adopted by Wintersteiner. They resemble glandular tubules, and consist of circles of 12–20 long cylindrical cells, with round or oval nuclei, 6–7 μ in diameter, situated in the club-shaped distal ends (Fig. 470). The cells taper slightly towards the lumen, and then broaden out to form a basal plate, which joins those of the neighbouring cells to form a continuous basal membrane. The lumen is 5–20 μ or more broad, often empty, but frequently containing the ordinary tumour cells. They also often contain small club- or rod-shaped clumps, which stain with protoplasmic stains, and are either free or attached by the smaller ends in a radial manner to

the cylindrical cells. The rosettes are not always circular, but often horse-shoe shaped or spiral. They never form long tubules, are always open at one end, and the ends are always curled in. There is always a highly refractile border on the concave side. The rosettes are irregularly distributed: they are often entirely absent, or present only in parts. They are commonest in the primary nodule, whether that be near the ora serrata or the optic nerve. Wintersteiner found them chiefly in a choroidal nodule in one case, in a non-vascular extension in the sub-retinal space in another, and once in an extra-bulbar tumour near the optic nerve when they were absent in the intra-ocular growth. They are commoner in the earlier than in the later stages. Transition forms between rosettes and the ordinary tumour elements occur. They consist of unipolar, club-shaped, or cylindrical cells arranged in small rosettes, with little or no lumen, no basal membrane, and less regularity of disposition.

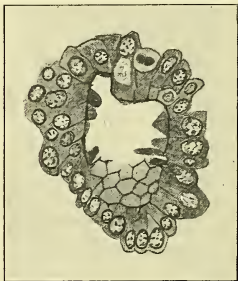


FIG. 471.—GLIOMA RETINÆ.
Verhoeff, R. L. O. H. Rep., xv. A rosette, showing limiting membrane in section and on the flat.

The rosettes are probably aggregates of rod and cone fibres: hence the basal membrane represents the membrana limitans externa (Fig. 471), the protoplasmic protrusions into the lumen the rods and cones, and the nuclei the outer granules. This view is supported by cases in which identical rosettes have been found in microphthalmic and other congenitally deformed eyes (B. Becker, Salzmann, Bernheimer, Rubinski, Helfreich, Dötsch, Pichler, E. v. Hippel, Wehrli) and in inflammatory conditions (Wintersteiner, Dötsch, Pichler, Ginsberg, Murakami, Pusey).

Wintersteiner found rosettes in 11 out of 32 cases of glioma. This must be looked upon as an exceptionally large proportion.

B. BECKER.—A. f. O., xxxiv, 3, 1888. SALZMANN.—A. f. O., xxxix, 4, 1893. BERNHEIMER.—A. f. A., xxviii, 1894. RUBINSKI.—Dissertation, Königsberg, 1890. HELFREICH.—A. f. O., xxi, 2, 1875. E. v. HIPPEL, A. f. O., lv, 3, 1903. DÖTSCH.—A. f. O., xlviii, 1, 1899. MURAKAMI.—A. f. O., liii, 3, 1902. PUSEY.—A. of O., xxxii, 1903. PICHLER.—Z. f. A., iii, 1900, Ergänzungsheft. GINSBERG.—Z. f. A., v, 1901. WEHRLI.—A. f. O., lx, 2, 1905.

(4) *Ganglion cells* (Virchow).—Large cells with long processes were met with by Virchow, and thought to be ganglion cells. Leber found similar cells, rich in protoplasm, much resembling Deiter's cells, and those found by Golgi in the brain. It has not yet been settled whether these are remnants of the ganglion cell-layer, or offspring of these cells, or hypertrophied neuroglia cells. The Golgi method is incapable of settling this point in pathological tissues, and the Nissl method should be applied, as suggested by Ginsberg.

Greeff first applied Golgi's chrome silver impregnation method to glioma retinae, and his results have been partially confirmed by Hertel.

The results obtained in pathological material by this method must be accepted with extreme reserve—indeed they are valueless unless supported by other methods. Greeff distinguishes three types of ganglion cells—giant, medium, and small. The giant type consists of large polygonal cells, six to eight times the size of spider cells, with numerous processes dividing dichotomously and ending in a rich terminal arborisation. These much resemble normal ganglion cells, but may be hypertrophied glia cells. In the medium type the cell body is round, oval, or angular, and the axis cylinder process has varicosities upon it. The small type consists of fibrils with oval, cell-like swellings, or of angular bodies with sparse processes. They resemble embryonic ganglion cells, the youngest, with a single process, being neuroblasts (His); these develop into bipolar and ultimately into multipolar cells. Hertel was only convinced of the medium type; the small ones he considered to be segments of varicose fibrils.

(5) *Neuroglia cells*.—The majority of the cells which stain by the Golgi method look like neuroglia cells or spider cells (Deiter's cells), with small cell bodies and multitudes of hair-like processes. They are present in large numbers. It is by no means improbable that they are simply artefacts. Scaffidi found that they failed to stain by any other known method of staining neuroglia.

(6) *Giant cells*.—These have been found by Vernon, Noyes, Becker, and others. They are uncommon, and capillaries with proliferated endothelium are readily confounded with them. Leucocytes, often with detritus and pigment within them, are seen, and all transition forms from them to giant cells are found (Wintersteiner). The latter are usually round or oval, with sharp, often irregular contour, little cytoplasm, and three to eight nuclei.

Proliferation.—Increase of the cells takes place by karyokinesis, which is most seen near the vessels (Mazza, Eisenlohr, etc.). da Gama Pinto also described indirect segmentation and fragmentation.

Stroma.—The intercellular substance appears clear, granular, or reticular in hardened sections. Wintersteiner holds that there is no true stroma, the fibrils being cell processes. That these are present in thick, bushy bundles, the individual fibrils of which do not anastomose, is probable from the investigations of Greeff and Hertel. They are not stained by Weigert's neuroglia stain, nor by Mallory's stain. Possibly they might stain by Benda's method, which is successful in pathological conditions of the optic nerve (Ginsberg). I have tried it, but as yet without success.

Degenerative changes.—One of the most characteristic features of glioma as compared with other growths is the extraordinarily early occurrence of degenerative changes, not only in the primary growth, but also in metastases, especially intra-bulbar ones. The probable explanation is that the growth is at first extremely slow, owing to the intra-ocular pressure, and is only rapid in the later stages (Wintersteiner); or it may be that the intra-ocular pressure tends directly to induce degenerative changes, since they are much less marked in the extra-ocular tumours.

The commonest change is *fatty degeneration* of the cells, which is

seen in its earliest form in the transition zone. Vacuoles appear in the nucleus, whereby the chromatin is pushed towards the periphery, or is broken up into irregular granules of various sizes, which often stain very deeply. The cells then much resemble polymorphonuclear leucocytes, and have often been mistaken for them (v. Graefe, Thalberg, Treitel). An apparently undoubted case of glioma associated with pus-formation has been recorded by Lenders: the diagnosis was supported by Leber. The chromatin granules are gradually absorbed and disappear, the cell then staining uniformly and deeply with eosin and other protoplasmic stains. The cells then seem to form a homogeneous mass, but round contour can always be made out in thin sections with a high power. Simultaneously with the nuclear changes fat droplets appear in the cytoplasm, and leucocytes containing fat can also be seen, distinguished by their size and sharp contour. When the fatty degeneration is very marked, the cells are broken up into a granular mass, resembling that produced by caseation, which formerly led to confusion with tubercular conditions. In these patches *cholesterin* crystals are of frequent occurrence. Myxomatous degeneration (Knapp) is probably an erroneous interpretation. Fatty degeneration and necrosis are apparently independent of vascular degeneration, though intimately related to the absence of capillaries. *Calcification* follows these changes in the primary growth filling the vitreous chamber; it never occurs either in local or distant metastases. The fine granules or concretions, which contain calcium carbonate or phosphate or both, stain very deeply with hæmatoxylin, and occur in the oldest degenerated spots, but may lie in close proximity with the young cells, for the same reasons that an intermediate zone is often absent. Calcification is invariable in the intra-ocular growth, except in the very earliest stages. The chalky granules have an organic basis, which is hyaline or granular in decalcified specimens. Bone formation was formerly described, probably inaccurately.

Hyaline degeneration is a rarer phenomenon: the round granules or masses stain deeply with eosin and acid aniline dyes, and are insoluble in acids and alkalis. They have been found in and between the cylindrical cells of the rosettes, usually about 6-8 μ in diameter, as well as in other parts.

Pigmentation (hæmachromatosis) occurs only as a sequel of hæmorrhage, and as such frequently in the primary nodules and in metastases. The golden or brown granules are found free in the tissues and detritus, as well as in leucocytes; they give the iron reaction. The glioma cells are always pigment-free. Microscopically epithelial pigment may also be seen, especially in the ciliary region, due to entrance or enclosure of pigment epithelial cells, or to transference by leucocytes. It is never a prominent feature.

TREACHER COLLINS.—Researches, London, 1896. NOYES.—Med. Record, xvii, 1880. VETSCH.—A. of O., xii, 1883. SALZMANN.—A. f. O., xxxix, 4, 1893. LEBER.—In G.-S., v, 1877. GREEFF.—Deutsch. med. Woch., xxii, 1896. HERTEL.—K. M. f. A., xxxv, 1897. VERNON.—R. L. O. H. Rep., vi, 1868. A. BECKER.—A. f. O., xxxix, 3, 1893. GINSBERG.—Grundriss, Berlin, 1903. *SCAFFIDI.—Virchow's Archiv, clxxiii, 1903. v. GRAEFE.—A. f. O., xiv, 2, 1868. THALBERG.—Dissertation, Dorpat, 1874. TREITEL.—A. f. O., xxxii, i, 1886. LENDERS.—A. f. O., lviii, 2, 1904. ALT.—Amer. J. of O., xxi, 1904.

The vessels.—In spite of the observations of the older investigators, and the striking appearances of sections, gliomata are relatively poor in blood-vessels, the spaces between them being relatively large. They consist merely of endothelial tubes with a thick cloak of connective tissue, in which muscle-fibres and elastic fibres are always absent. They therefore resemble capillaries with extremely wide, but variable, lumen (12–36 μ , Hirschberg). The presence of dilatations, leading to slowing of the blood-stream, is not unimportant as a factor in the malnutrition of the tumour (Wintersteiner).

Regressive metamorphoses are common. *Hyaline degeneration* of the walls commences with thickening of the connective tissue, which often shows concentric lamination or radial striation. Later the endothelium becomes vacuolated and disappears, or also undergoes hyaline changes. Finally all the nuclei disappear, and the vessel in section is merely a homogeneous ring of variable breadth, in which the blood may be normal or coagulated, eventuating in the formation of a hyaline thrombus. Hyaline degeneration only occurs in the primary tumour, and not in intra- or extra-bulbar metastases.

More rarely *calcification* of the vessels is found, generally as a sequel of hyaline degeneration, but also in quite unaltered vessels, in which case it may occur in extra-bulbar growths. In the former case the hyaline ring has a dark blue (hæmatoxylin) calcareous outer edge, which fades off centrally; or the endothelium may calcify, or the wall may calcify *en masse*. Both hyaline degeneration and calcification are best seen in the intra-vitreous vessels and in the anterior parts of the retina.

Thrombosis, endarteritis, and periarteritis occur in the extra-ocular growths, rarely in the primary growth. *Hypertrophy* of the media and adventitia is also seen in the ciliary arteries before they enter the globe in late cases with glaucoma fully established (Wintersteiner). *Necrosis* of the vessels of the primary tumour (Jung) and of the central vessels of the retina (Wintersteiner) may happen.

The vessels arise from those of any organs in which the tumours grow. Convolted vessels occur in the ciliary region and anterior part of the vitreous, showing marked degeneration, and often having no sheaths of tumour cells. They are probably persistent fœtal vessels (Wintersteiner).

Whilst the primary growth is relatively poor in vessels, these are much more numerous when rapid growth and metastasis begin, especially in the uveal tract. In the cornea and sclera, where vessels are normally scanty, the growth is poorly supplied, and it is altogether free from vessels in extensions between the lens fibres. Non-vascular nodules, never large, occur in the pigment epithelium, between it and the lamina vitrea, in the vitreous, in the zonule, and in the posterior and anterior chambers; they are nourished by diffusion, and the central cells rapidly necrose, so that the nodules stain as blue rings with a red centre (hæmatoxylin and eosin). Extra-ocular growths are usually rich in vessels, but the tubular structure may also be seen here.

There is no good evidence of perivascular lymph sheaths, though such have been described (Brailey, Bull, Straub): the tumour cells,

indeed, are very intimately united to the vessel walls, so much so that da Gama Pinto thought they were outgrowths of the adventitia.

Hæmorrhages have always been considered a prominent feature in gliomata: they vary enormously in size, shape, etc., but are usually many and small, and occur most near the thin endothelial vessels and the calcified ones, less near hyaline ones.

BRAILEY.—R. L. O. H. Rep., x, 1881; also viii, 1874-6; ix, 1876. BULL.—T. Am. O. S., 1892. STRAUB.—A. f. O., xxxii, i, 1886.

Origin and propagation.—The researches of v. Graefe, Hirschberg, and Knapp definitely proved the retinal origin of glioma. It arises about four times as frequently in the posterior part (51 : 12, Wintersteiner), and generally below (medial 6, lateral 18, below 21, above 4).

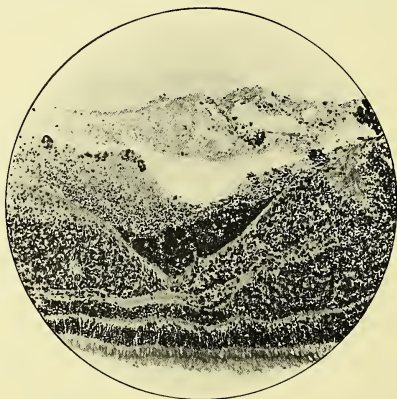


FIG. 472.—GLIOMA RETINÆ.

From a photograph by Lister. Showing the nuclear layers spreading out on the right into the growth.

The resemblance of the cells to the nuclear layers early pointed to these as the starting-point (Robin, Horner and Rindfleisch):—the inner layer—Schweigger, Hirschberg; the outer layer—v. Recklinghausen, Virchow. Manfredi cited a case arising “from the nuclei at the base of the radial fibres, described by Kölliker.” Iwanoff found another arising in the nerve-fibre layer (also Hirschberg, Brailey, Wintersteiner). Wintersteiner gives the following table of origin in the few cases in which it can be asserted with probability:

(a) From the nerve-fibre layer	.	.	.	.	5
„ „ inner nuclear layer	.	.	.	.	19
„ „ inner layers chiefly	.	.	.	.	12

(b) From the outer nuclear layer	9
„ „ outer layers chiefly	3
	— 12
(c) From the nuclear layers (either both or without further details)	6
	— 6

Glioma therefore arises much oftener—about three times—from the inner than from the outer layers of the retina; but it probably arises from various layers, not only in different cases, but also in the same case (Leber). It is important to note that the terms endo- and exophytic have nothing to do with the layers of the retina (erroneously Brailey, Knapp, v. Michel), but only with the direction of growth.

In all the published cases the tumours are multiple even in the earliest stages, though one growth is larger than the others and may be called with probability the primary growth. That some of the others are also independent nodules, and not local metastases, is probable, especially when one remembers that in a fifth to a fourth of all the cases there has been a glioma in the other eye, and in nearly all of these it is practically certain that it was an independent growth. At the same time, different specimens vary much in appearance, from an apparently single large tumour to a plentiful sprinkling of the whole retina with “miliary” growths of various sizes.

The extension of the growth in the retina itself takes place in two ways: (1) by proliferation of the primary growth; (2) by the deposition of local metastases, which are gradually overtaken and absorbed by the primary growth. The cells proliferate by karyokinesis, and extend almost entirely along new-formed vessels by the methods already mentioned. The formation of metastatic satellites is a characteristic phenomenon which is almost, if not quite, unknown in other intra-ocular growths. Cells of the primary growth break off and float free in the vitreous or subretinal space, where they continue to grow. In this manner they are sown upon the retina around the primary growth and produce subsidiary tumours. The cells are carried to more distant spots in the eye and in the body generally both by the lymph and by the blood.

By the lymph-vessels the cells grow along the blood-vessels, which have perivascular lymph-sheaths in the retina; and in the same way perforate the sclera along the anterior and posterior ciliary vessels, penetrate the optic nerve along the central vessels, and get into the choroid along the anastomoses which these make with the ciliary vessels around the nerve.¹ By the lymph-stream they are carried to the anterior and posterior chambers, Tenon’s capsule, the intervaginal space, and farther afield to the glands of the parotid region, neck, and mediastinum.

The cells also enter the blood-vessels, as has been proved by metastatic deposits inside the capillaries of the liver, the walls of the vessels and the liver cells being intact (Bizzozero). The cells have been described inside the vessels of the eye and of the growth (Wintersteiner, Nattini).

¹ See PARSONS, ‘The Ocular Circulation,’ London, 1903.

The distribution of extra-ocular metastases is indicated in the following table:

Brain and membranes	43 times
Skull and bones of the face	40 "
Lymphatic glands	36 "
Parotid (probably lymphatic)	9 "
Skeletal bones	9 "
Liver	7 "
Spinal cord and membranes	5 "
Kidneys	2 "
Ovary	2 "
Lungs	1 "
Spleen	1 "

(Wintersteiner).

The choroid is usually first affected after the retina, groups of cells being found in the meshes of the middle and outer layers, and in the suprachoroidea. In the majority of cases the choroid is first affected near the optic nerve, probably along the anastomosing vessels, as mentioned (Wintersteiner). Groups or layers of cells are often found under the retinal pigment epithelium, lying upon Bruch's membrane. The latter is always perforated in places in the late stages, and invasion of the choroid has been attributed to this path (Grolmann). The perforations, however, are never present in the early stages, and are due to the growth of the tumour in the choroid, as in other choroidal growths. Choroidal metastases often occur without deposits on the lamina vitrea, and *vice versâ*. Another method of invasion of the choroid is by new-formed vessels passing directly from the retina into the choroid near the ora serrata (Schweigger, Hirschberg, Bochert, Baumgarten, Nattini). Such vessels are never present normally (Leber).

The optic nerve is next affected—always by continuity, very rarely before the choroid (Knapp). The nerve-fibres degenerate as the result of the retinal growth, and the tumour cells make their way through the spaces in the lamina cribrosa, and then proliferate rapidly in the looser tissue beyond. They often become spindle-shaped here. They also pass along the perivascular lymph spaces. The septa of the optic nerve remain for some time, only disappearing gradually as the nerve is replaced by growth. Occasionally the tumour breaks through from the papilla into the intervaginal space and proliferates there, the nerve proper only being attacked secondarily and late; in the early stages it is then free from growth, and is thin and atrophic. When the nerve of the opposite eye is affected by way of the chiasma, the growth attacks it from the vaginal sheath.

The anterior chamber may be attacked by growth forwards of the choroidal tumour; by continuity through the zonule of Zinn, which is destroyed; or often by local metastases, isolated cells or cell groups being carried into the angle by the lymph-stream. Hypopyon may be simulated by the last method, as I have seen (Fig. 232, Vol. I). It is not due to cells extruded from the iris, as suggested by Jessop. The anterior chamber may also be attacked by continuity from deposits in the iris, themselves derived from the choroid *viâ* the ciliary body. Hyphæma may also

occur—always in the glaucomatous stage (Hulme, Hirschberg, Bochart, Becker, etc.); it fortunately occasioned the removal of an eye recently which otherwise had all the clinical features of pseudo-glioma.

Perforation of the globe takes place along the perforating vessels— anterior ciliary, vortex veins, and posterior ciliary—most commonly near the optic nerve, with diminishing frequency from behind forwards. Isolated perforation through the sclerotic just behind the cornea has been described by Wadsworth, Vetsch, Grolmann, and others. The sclera may be directly attacked from the suprachoroidea, or the inner laminae may be burst by the raised intra-ocular tension and then attacked. Growth is enormously rapid in the loose orbital and subconjunctival tissues, so that the orbit is soon filled, and the tumour grows forwards between the lids.

HORNER AND RINDFLEISCH.—K. M. f. A., i, 1863. SCHWEIGGER.—A. f. O., vi, 2, 1860. MANFREDI.—Riv. clinica, 1868. BIZZOZERO.—Moleschott's Untersuchungen, xi, 1871. NATTINI.—Ann. di Ott., xxii, 1894. GROLMANN.—A. f. O., xxxiii, 2, 1887. BAUMGARTEN.—A. f. O., xxii, 3, 1876. HULME.—Trans. Path. Soc., ix, 1858. WADSWORTH.—T. Am. O. S., 1873. SEYDEL.—K. M. f. A., xxxviii, 1900. SYNDACKER.—A. of O., xxx, 1901. JESSOP.—Ophth. Rev., xxii, 1903.

Changes in other parts of the eye. *Retina.*—In glioma exophytum the retina is invariably detached. Detachment occurs unusually early in these growths, and is quickly very extensive, either being umbrella-shaped, or forming a thick axial band from the disc to the posterior pole of the lens. In glioma endophytum the retina remains wholly or mostly *in situ*.

There are nearly always atrophic changes in the retina, which is generally reduced to a thin fibrous membrane, in which only the nuclear layers, often reduced to a single one, remain recognisable. The earliest evidences of degeneration are thickening of the supporting fibres, thinning and necrosis in the nuclear layers, swelling and breaking up of the rods and cones, disappearance of the ganglion cells, and degeneration of the nerve-fibre layer. The subretinal space is filled with an albuminous fluid, which contains leucocytes in small numbers in all stages of degeneration, red corpuscles, pigment cells and granules, blood-pigment, cholesterin crystals, etc. This fluid is a transudate rather than an inflammatory exudate: it is usually coagulated in hardened specimens.

Vitreous.—The vitreous remains clear for a long time, and is often the seat of metastatic deposits, especially and characteristically in glioma endophytum. These form small floating nodules, which never contain blood-vessels. Later the vitreous shrinks, and is represented in sections only by a homogeneous, fibrillar, or granular mass behind the lens. There is occasionally a thin membrane, poor in vessels, stretched across behind the lens, and this may be the cause of difficulties in diagnosis clinically.

Pigment epithelium.—The pigment epithelium degenerates early, the cells becoming flatter, and partially or wholly depigmented. The pigment granules are taken up by leucocytes, which are usually much swollen. The pigment cells become vacuolated, and show every transition to the formation of so-called "colloid" bodies of the choroid,

Nattini describes hyaline and fibrillar thickenings of Bruch's membrane resembling capsular cataract. The pigment epithelium also proliferates in places, forming heaps, or commonly a double layer. Evascular metastatic deposits occur on and under the epithelium, either as nodules or flattened laminæ. The epithelium may be quite normal over these, so that the growth has burrowed beneath it, or it may have proliferated over the growth, degenerated epithelium in this case being found beneath the deposit (Bochert). These metastases never pierce the lamina vitrea (*cf.* Delafield), but grow inwards, and never attain great size owing to the absence of vessels. The pigment can often be made out as a dark line between the retinal and choroidal growths even when the globe is filled with the tumour: here the pigment cells have disappeared, but the pigment granules remain *in situ*, imprisoned in round or spindle-shaped cells.

Choroid.—The choroid first atrophies, and that early: the degenerative changes resemble those found in glaucoma, but are present before the glaucomatous stage arrives, and are due to disordered nutrition. The pigment cells are scanty, but this is probably due to arrested development and not to degeneration, since the choroid is normally unpigmented in the new-born. Metastasis occurs early, and attacks an atrophic organ. The youngest deposits are found in the outer layers, amongst the large and medium-sized vessels, rarely in the suprachoroidæa. The cells form rows and lens-shaped aggregations between the planes of the supporting tissue, infiltrating Sattler's layer, avoiding the choriocapillaris, which may have atrophied, and projecting towards the sub-retinal space, but always as a diffuse thickening, never as a circumscribed tumour. The suprachoroidal space is always obliterated, the choroid never being detached. The thickening of the choroid may be considerable (1 cm. or more) before the lamina vitrea gives way: even then the choroidal growth is distinguished by its striped appearance, due to the arrangement of the cells between the laminæ. In later stages the typical tubular structure is seen. Changes in the vessel walls are exceptional. As already mentioned, metastasis usually occurs at the posterior pole first, and is multiple, with subsequent confluence: it is therefore a true metastasis, and not merely extension by continuity. Tumour cells may invade the capillaries and form malignant thrombi. Inflammatory processes are absent or quite subsidiary.

Iris (*see* also Vol. I, p. 331).—The atrophic changes in the iris are those found in all glaucomatous conditions—peripheral anterior synechia, atrophy of the stroma, ectropion of the pigment epithelium and sphincter, macroscopic vascularisation, etc. Involvement in the growth is usually late: the iris may be imbedded and yet not infiltrated; more frequently it is attacked from the ciliary body, leading to iridodialysis (da Gama Pinto), rarely visible clinically (Vetsch). Evascular metastatic deposits occur under the pigment epithelium, quite analogous to those on the choroid. The pupillary edge of the iris is often some distance (*e.g.* 1 mm.) in front of the lens in cases with broad adhesion of the iris to the cornea at the periphery; the absence of iridodonesis is probably due to narrowing of the free area.

Anterior chamber (see also Vol. I, p. 331).—Metastatic deposits in the angle occur, and may simulate hypopyon (v. p. 638). Usually the chamber is normal until glaucoma supervenes, when the ordinary features of that condition are present. Deepening of the chamber is rare (Story, da Gama Pinto).

Ciliary body.—Atrophy is common early, and may be excessive, so that the ciliary body is thinner than the choroid. It consists of dense connective tissue, poor in vessels, and apparently rich in pigment. The ciliary processes are elongated, and are pushed or pulled forwards. Later the ciliary body is regularly involved in the growth and replaced by it, its contour only being marked out by a line of pigment. It is usually attacked from the choroid; but it may be attacked from the suprachoroidal space, or from the inner surface. Finally, the ciliary processes succumb, and no trace of the ciliary body remains. In the rare cases in which the globe shrinks the ciliary body may be detached.

Lens.—The changes in the lens are peculiar, and may be considerable without affecting its transparency. Wintersteiner found only 3 normal—and those amongst the youngest cases—out of 32. It is at first in its normal position; later it is pushed forwards, and altered in shape, being either flatter or rounder than normal. Still later it becomes partially absorbed, and also deformed by pressure. Finally only the capsule may remain, or even this may disappear. In the early stages the epithelium extends beyond the equator, and may line the posterior capsule in one or more layers. The cells, from being cubical, become flattened and often spindle-shaped; they also show flattening, vacuolation, and localised proliferation beneath the anterior capsule. Later the appearances of a very extensive, flat anterior polar cataract are seen (in a fifth of the cases, Wintersteiner). More rarely the epithelium disappears entirely. Under the capsule is a very characteristic homogeneous zone—hydrops subcapsularis lentis. Adjoining this the fibres show ordinary cataractous changes—clefts with exudates and hyaline globules, etc. Absorption seems to occur from without in. Wintersteiner in five cases confirmed a unique observation of Bochart's. There was a dark blue zone in the peripheral layers when stained with hæmatoxylin and eosin: there were innumerable dark globules, varying in size from cocci to leucocytes, insoluble in acids and alkalis (hyaline degeneration). Calcification occurs rarely. Involvement in the growth is relatively uncommon, but it occurs, the cells filling the spaces between the fibres, isolating and replacing them.

Cornea.—The cornea is stretched (keratomegalie, Parent) and thinned. Multiple ruptures of Bowman's membrane, filled in with short spindle cells, are common, those of Descemet's membrane rarer, but quite characteristic when they occur. Ulceration follows lagophthalmia, and leads to perforation, with proliferation of the growth through the wound. Vascularisation of the cornea, with interstitial hæmorrhages, is seen. Involvement of the cornea in the growth occurs late, usually *viâ* the ligamentum pectinatum, but also through ruptures of Descemet's membrane, at the edges of a perforation, etc.

Sclerotic.—The sclerotic is usually stretched, thinned, and locally ectatic. The staphyloma is commonly ciliary, very rarely posterior.

GLIOMA RETINÆ ASSOCIATED

Case.	Author.	Sex.	Age.	Eye.	Other eye.	Duration of disease.	Clinical condition.
1	Sichel	?	3	R.	Glioma	—	Amaurotic cat's eye
2	Knapp	M.	1 $\frac{3}{4}$	R.	?	8 days	Inflammation; protrusion; perforation; second perforation in 3 months; shrinking
3	Hirschberg and Happe	F.	20 weeks	R.	Glioma	20 weeks	Hyphæma; shrunken globe
4	Wadsworth	M.	14 months	L.	Blindness	8 months	Inflammation; swelling, then shrinking
5	Armaignac	F.	26 months	R.	?	10 months	Shrunken globe; perforation
6	Snell	?	21 months	R.	Glioma	3 months	Shrunken globe
7	Brailey	F.	9 months	L.	Glioma	—	Painful; shrinking; hyphæma
8	Brailey	F.	26 months	R.	Glioma	10 months	Panophthalmitis; shrinking
9	Lawford and Collins	M.	9 months	L.	Glioma	—	Shrunken globe
10	Lawford and Collins	M.	2	L.	Glioma	—	Shrunken globe
11	Collins	M.	16 months	L.	Glioma	15 months	Shrunken globe
12	Lukowics	M.	18 months	L.	—	15 months	Varied in size; perforation
13	Marshall	F.	5	R.	Glioma	4 years 9 months	Glioma; in 3 years and 9 months shrinking
14	Lagrange	F.	7	L.	—	18 months	Inflammation and shrinking
15	Parsons	F.	18 months	R.	Glioma	10 months	Shrunken globe

WITH SHRINKING OF THE GLOBE.

Operation.	Result.	Macroscopic examination.	Microscopic examination.
<i>Nil</i>	Marasmus; death	White tumour of retina; optic nerve normal	<i>Nil</i> .
Enucleation	Recurrence (extirpated); death	Red mass with hæmorrhage	Glioma.
Enucleation	No recurrence; death	Growth on nasal side anteriorly	Glioma.
Enucleation	Recurrence; death	Filled with growth; extra-ocular growths; optic nerve enlarged	—
Enucleation	Recurrence; death	Large growth in orbit	—
Enucleation	Death	"Undoubtedly glioma"	—
Enucleation	—	Thickened detached retina	? Glioma.
—	Growth in left and metastases	—	—
Enucleation	?	Shrunk globe; choroidal inflammation; infiltration (? inflammatory) of nerve	? Glioma.
Right eye enucleated	?	Not examined	—
Both enucleated	—	Full of grey substance; lens absent	"Typically gliomatous."
Exenteration	No recurrence in 3½ months	Globe full of tumour	Glioma.
Both enucleated	—	White mass in vitreous	Glioma.
Enucleated	No recurrence in 2 years	Filled with growth	Glioma.
Enucleated	Death	White mass in vitreous	Glioma.

Anterior (corneal) staphyloma is always due to ulceration (ophthalmia neonatorum, etc.), and is not directly dependent upon the glioma. The sclerotic is attacked by the growth along the perforating vessels, and it also invades the interlamellar spaces. The lamellæ are very resistant, and remnants persist almost indefinitely.

Optic nerve.—The optic nerve early degenerates as the result of the growth in the retina and of the atrophy and detachment of that structure. The lamina cribrosa becomes bowed backwards and the optic disc cupped by the secondary glaucoma, either before or after (Wintersteiner) the detachment of the retina. The cup is invariably filled in with new growth, so that in most cases which come under observation both atrophy and invasion by the tumour are present. The cup is more usually ampulliform than simply cylindrical. The modes of invasion have already been mentioned. In a rare case Wintersteiner found extensive necrosis of the nerve, probably from the pressure of an orbital mass upon the vessels. The growth in the nerve degenerates early in the centre, owing to the absence of vessels in the degenerated nerve and in the tumour itself.

Atrophia bulbi.—I have collected from the literature 14 cases of glioma of the retina associated with shrunken globe, and have recorded another case, so that there are now 15 cases on record. The principal points of interest in these cases are briefly set out in the table appended. It is unnecessary to enter into further detail since the most important have been published in English and are readily accessible.

It will be noticed that in no less than 10 of the cases it is stated that the other eye was the seat of glioma, in another case this eye was blind, whilst in the remaining four the condition of the other eye is not stated, so that it may be safely concluded that it was normal. In several of the cases there is no doubt that the eye became perforated before the onset of the shrinking, usually as the result of extra-ocular extension of the growth. In the other cases it is almost impossible to decide whether perforation occurred or not; it is a difficult point to settle in a shrunken eye on pathological examination alone. There have often been inflammatory symptoms preceding the atrophía bulbi, and it is probable that the shrinking is due to this rather than to any inherent tendency in the growth itself (Brailley), comparable with atrophic scirrhus; such an occurrence must be so rare as to almost negative the hypothesis. I am still of the opinion that the gliomatous nature of the cells in these shrunken eyes is not placed absolutely beyond cavil.

SICHEL.—Iconographie ophthalmologique, 1859. KNAPP.—Die intraoculare Geschwülste, Karlsruhe, 1868. HIRSCHBERG AND HAPPE.—A. f. O., xvi, 1, 1870. WADSWORTH.—T. Amer. O. S., 1873. ARMAIGNAC.—Jl. de Méd. de Bordeaux, 1878. SNELL.—T. O. S., iv, 1884. BRAILEY.—T. O. S., iv, 1884; v, 1885. LAWFOORD AND TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1, 1890. TREACHER COLLINS.—R. L. O. H. Rep., xiii, 3, 1892; T. O. S., xvi, 1896. LUKOWICZ.—Dissertation, Halle-Wittenberg, 1884. MARSHALL.—R. L. O. H. Rep., xiv, 1897. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. *PARSONS.—R. L. O. H. Rep., xvi, 2, 1905.

Temporary retrogression in glioma retinæ is a cognate question which is of considerable interest. Such cases appear most frequently

in the earliest reports, probably owing to the fact that the need for immediate operation was not recognised (Wintersteiner). Almost invariably the tumour commenced to grow again rapidly at a later date, and the few cases in which this did not occur may be reasonably considered to have been errors in diagnosis. The difficulties in the differential diagnosis of glioma from pseudogliomata of various kinds are often so great as to be insuperable. Many of these cases show temporary diminution of intra-ocular tension and distinct tendency to shrink, without however going on to complete atrophy of the globe. They therefore represent a group very nearly allied to the cases just discussed, and are of great importance in demonstrating that quite undoubted gliomata may show signs of shrinking at some stage of their history.

Including the cases of complete atrophía bulbi, Lagrange has collected 21 cases which showed temporary retrogression. The cases reported by Tyrrell, Rolland, Knapp, and Grolmann are particularly interesting in that they showed alternate tendencies to shrink and to grow. The most striking is Grolmann's case. Here a child, æt. 6, had had the right eye removed for glioma four years previously. The left then showed a grey reflex; no vessels could be seen. After two days' treatment with inunctions the mass diminished in size, and in seventeen days it could only be seen with the pupil dilated. Five weeks later numerous yellow nodules were seen floating in the vitreous, and two months afterwards the tumour commenced to grow, accompanied by inflammatory symptoms. Hypopyon appeared, which was repeatedly evacuated, but recurred. The growth increased until it reached the lens, glaucoma setting in; then the cornea became ectatic. Finally, the tumour filled the anterior chamber, perforated the cornea, and grew rapidly outside the globe. In about a month the child died, the disease having lasted in this eye for eleven months. It will be noticed that this eye never shrank.

WINTERSTEINER.—*Das Neuroëpithelioma Retinæ*, Leipzig and Wien, 1897. HAYES.—*Medical Observations and Injuries*, iii, London, 1767. WELLER AND V. AMMON.—*Die Krankheiten des menschlichen Auges*, Berlin, 1830. TYRRELL.—*Diseases of the Eye*, 1840. V. GRAEFE.—*A. f. O.*, x, 1, 1874. GROLMANN.—*A. f. O.*, xxiii, 2, 1887. ROLLAND.—*Rec. d'O.*, 1889. SCHÖBL.—*C. f. A.*, xx, 1896.

The nature of glioma retinæ.—Our knowledge of glioma is still insufficient to permit of dogmatism as to its exact nature. The superficial resemblance to small round-celled sarcoma early led to its being included in this category. Minute examination dissipates the resemblances; moreover, the origin of a sarcoma in a purely epiblastic structure—the vessels only excepted—is contrary to present pathological views.

Virchow instituted the term "glioma," on the grounds that the supporting tissue of the retina afforded the matrix of the growth. Recent investigations, whilst they have modified this opinion in details, are not inconsistent with it, and the term may well be retained in preference to others which involve more doubtful conjectures.

Wintersteiner, in his exhaustive researches, was fortunate in finding rosettes in an unusually large proportion of cases. He looks upon

them as the key to the mystery, the germ of the growth—a germ which is derived from the outer layer of the retina, and, like one of Cohnheim's "rests," is planted in other parts of the organ. He therefore adopts Flexner's term "neuroëpithelioma." On general grounds of the epiblastic origin of the neoplasm there is no objection to this term; but Wintersteiner restricts its meaning, so that it involves a theory which cannot be held to be fully proved. If it be granted that rosettes are derived from the neural epithelium, and are not merely islands of neural epithelium which have been caught and surrounded in the growth, and thereby modified, there yet remains the explanation of the majority of cases in which they are absent (21 cases out of 32, Wintersteiner). In many of these the tumours may be too far advanced, but rosettes are not invariably found in the younger ones. Moreover, if the main mass of the glioma cells consists of rod and cone bipolars, it is curious that proliferation of the inner nuclear layer should

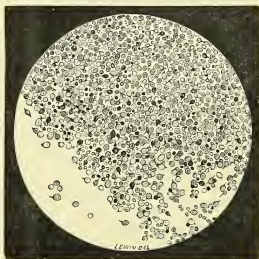


FIG. 473.—GLIOMA RETINÆ.

Treacher Collins, Researches. Microscopical appearances of glioma of the retina, for comparison with Fig. 474.

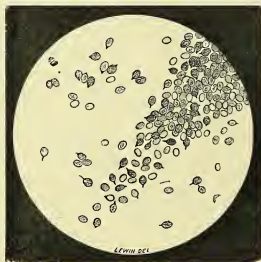


FIG. 474.—FETAL RETINA.

Treacher Collins, Researches. Microscopical appearances of the retina from a human fœtus between the third and fourth months.

be commoner than that of the outer. There are many difficulties in the way of accepting Wintersteiner's theory, and since he has restricted the use of the attractive term "neuroëpithelioma," one is compelled regretfully to avoid it altogether.

Greiff also has recourse to Cohnheim's theory. He deduces from his investigations the conclusion that the main mass of the growth consists of neuroglial spider cells. These are normally present only in the ganglion cell and nerve-fibre layers. Misplaced cells, however, are not uncommon in the retina (especially in birds, Ramón y Cajal). Greiff, therefore, thinks that the tumour originates in a ganglionic and neuroglial "rest," and introduces the term "neuroglioma ganglionare."

Treacher Collins has pointed out the resemblance of glioma cells to those of the undifferentiated retina of the fœtus at about the third month. The retina then consists entirely of a mass of round cells with large nuclei and scarcely any protoplasm, some however having

little spicules projecting from them (Figs. 473, 474). The resemblance suggests that just as sarcoma represents the foetal condition of the tissue from which it primarily grows, so glioma represents the foetal condition of the retina.

Axenfeld also points out the possibility of the development of both glia cells and ganglion cells from the undifferentiated cells of the tumour, and Ginsberg has elaborated this idea. He considers that the elements of the rosettes are not neural epithelium, but embryonic cells which have not yet been differentiated into spongioblasts and neuroblasts. According to the researches of Schwalbe and of Falchi the cylindrical cells of the pars ciliaris retinae belong to this category, and



FIG. 475.—INTRA-OCULAR GROWTH.

Treacher Collins, T. O. S., xii. Described as a vascular retinal growth; probably a perithelioma of the choroid.

these much resemble those of the gliomatous inclusions. In favour of Wintersteiner's view that the rosettes are the primary germs of the tumour, he points out the frequency of mitoses around them, though in the secondary tumours these are numerous in the ordinary round cells. On the other hand, it is possible that the rosette cells do not possess their characteristic features from the beginning, retaining and reproducing them, but that these develop from undifferentiated germs in the course of proliferation. The occurrence of rosettes in extra-retinal metastases shows that they are not entirely "rests." On the whole, this theory is the most comprehensive and the most philosophical. It has been adopted by Emanuel, who re-names the tumours "diktyomata."

Lagrange admits the occurrence of: (1) neuromata, corresponding

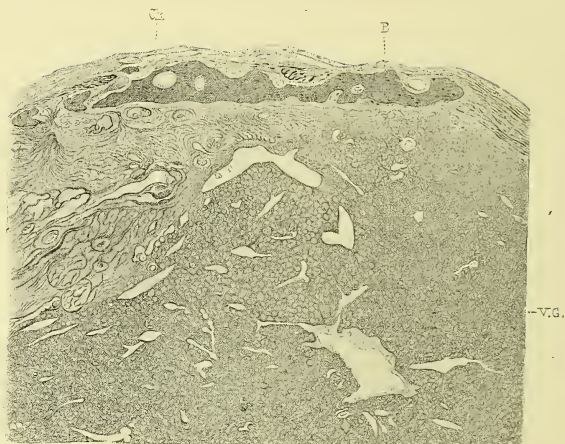


FIG. 476.—VASCULAR NEW GROWTH OF THE RETINA.

Treacher Collins, T. O. S., xiv. From the right eye of Case 2. V. G. Vascular growth. Ch. Choroid. B. Bone in choroid.



FIG. 477.—VASCULAR NEW GROWTH OF THE RETINA.

From the same specimen; higher magnification. C. V. Capillary blood-vessel. C. Large cells with their protoplasm marked out in a honeycomb fashion.



FIG. 478.—VASCULAR NEW GROWTH OF THE RETINA.

The left eye of the same patient. C. O. Position of cornea. B. C. Blood-clot. O. N. Optic nerve.

with Greeff's ganglionic neurogliomata; (2) neuroepitheliomata, having rosettes; (3) tubular angiosarcomata; and (4) round-celled sarcomata.

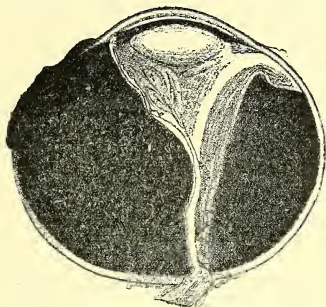


FIG. 479.—INTRA-OCULAR "MELANOMA."
Griffith, T. O. S., xiv. Macroscopic appearance.

This is rather begging the question: whether the last two groups occur is doubtful (*v.* p. 650).



FIG. 480.—INTRA-OCULAR "MELANOMA." $\times 50$.
From the same specimen. Microscopic appearance.

A few words must be said as to the relationship of retinal glioma to glioma of the central nervous system. The latter is distinguished by a

much lower grade of malignancy. The former occurs only in young children, and is very different in structure, possibly due in part to poorer blood supply and in part to the high intra-ocular pressure (Wintersteiner, Greeff). Epithelioid cells, reminiscent of those lining the central canal, also occur in brain gliomata. It must be remembered that the epithelium lining the central canal consists of spongioblasts (His), and differs essentially on current theories from the rods and cones; embryologically, however, the differences are small. On



FIG. 481.—INTRA-OCULAR "MELANOMA." $\times 350$.
From the same specimen; higher magnification.

the whole, the diversities between the two types of growth are well marked, and the identity in terminology is unfortunate.

TREACHER COLLINS.—*Researches*, London, 1896. AXENFELD.—In Lubarsch and Ostertag, *Ergebnisse*, etc., Wiesbaden, 1901. GINSBERG.—*A. f. O.*, xlviii, 1, 1899; *Z. f. A.*, v, 1901. KOERBER.—*Z. f. A.*, viii, 1902. EMANUEL.—*K. M. f. A.*, xli, 1903, Beilageheft.

OTHER PRIMARY TUMOURS OF THE RETINA

Glioma is the only primary tumour known to arise from the nervous elements of the retina. Since, however, the retina contains blood-vessels there is no inherent improbability of the occurrence of growths of mesoblastic origin. A few primary retinal tumours other than gliomata have indeed been described: all are open to question, some being almost certainly gliomata (*e.g.* Schöbl), others being inflammatory (Goldzieher, Nuel, Johnson), *e.g.* tubercular (da Gama Pinto), in origin, and others, again, growths involving the retina secondarily (Salzer). Salzer's case is interesting in that an angiosarcoma of the optic nerve invaded the papilla and surrounding retina, causing a well-marked intra-ocular tumour.

Treacher Collins (1892) published a case of intra-ocular neoplasm of doubtful nature and origin, which appeared to spring from the retina. The whole of the interior of the globe was filled with a fawn-coloured mass containing hæmorrhages. I have examined the sections and the macroscopic specimen of this case, and have pointed out the resemblance to a peculiar group of choroidal sarcomata with extensive necrotic changes (*v. p.* 526). The tumour is a typical angiosarcoma (perithelioma) (Fig. 475), and I have little doubt that it springs from the choroid, though this has not been proved beyond dispute; the author of the report now concurs in this opinion.

Treacher Collins (1894) has also published two other cases, in which both eyes of a brother and sister showed evidence of primary vascular growths (*angiomata*) of the retina; three of the eyes were examined microscopically. All three eyes showed extreme inflammatory and degenerative changes, both of the sister's eyes containing bone in the choroid. The retinal vessels were greatly dilated (*see* ophthalmoscopic picture, Wood), and large masses showing angiomatous structure were found, apparently springing from the retina. Although the conditions do not resemble ordinary inflammatory deposits, such an origin cannot be excluded (Figs. 476-8).

John Griffith has published another case, which he considered to be a retinal *melanoma*, springing from the retinal pigment epithelium, and comparable with the melanomata found in the iris. The tumour occurred in a man *æt.* 37; it was very extensive (Fig. 479) and undoubtedly malignant, since the tumour recurred in the orbit after excision of the globe, and the patient died within a year; there was no *post-mortem* examination. The tumour was very deeply pigmented, the pigmented cells having a tubular arrangement in parts (Figs. 480, 481); it was very vascular, and contained cystic spaces. The pigment was not tested for iron. The author, from an examination of the cells in bleached sections, came to the conclusion that they were epithelial. It is more probable, however, that the tumour was a sarcoma of the choroid, with somewhat exaggerated proliferation of the retinal pigment epithelium.

LEBER.—In G.-S., v, 1877. PAGENSTECHER AND GENTH.—Atlas, 1878. NUEL.—Ann. d'Oc., lxxxii, 1879. GOLDZIEHER.—K. M. f. A., xvii, 1879. SALZER.—A. f. O., xxxviii, 3, 1892. SCHÖHL.—C. f. A., xvii, 1893. WOOD.—T. O. S., xii, 1892. TREACHER COLLINS, T. O. S., xii, 1892; xiv, 1894. JOHNSON.—T. Am. O. S., 1897. *PARSONS.—T. O. S., xxv, 1905.

CHAPTER XI

THE OPTIC NERVE

THE NORMAL OPTIC NERVE

THE so-called optic nerve, together with certain parts of the retina, constitutes a lobe of the brain, and has therefore the characteristics of the central nervous system.¹ Hence the nerve-fibres are devoid of a sheath of Schwann, and the interstitial substance is neuroglia. It differs in detail from other parts of the brain, more particularly in the greater development of the interstitial neuroglia in its orbital portion.

The optic nerve may be divided into three parts: (1) the intracranial part, extending from the chiasma to the optic foramen; (2) the intra-orbital part, including the intra-canalicular part within the optic foramen, and extending to the globe; (3) the intra-bulbar part, including the intra-scleral part and the papilla. In the orbit the nerve is surrounded by three sheaths, derived from the membranes covering the brain.

The sheaths.—The three sheaths are the dural, the arachnoidal, and the pial; they are separated by two lymph spaces, the subdural and the subarachnoid, which are often spoken of together as the inter-vaginal space. The dural sheath is covered by an extension of Tenon's capsule, which is separated from the sheath by the supravaginal space. All the spaces are traversed by numerous strands of connective tissue, and they are all lined with endothelium, which also covers the linking strands. The endothelium sometimes forms laminated masses resembling the bodies found in psammomata.

The *dural sheath* consists of dense fibrous tissue, richly supplied with elastic fibres, and containing scattered flat cells, as well as vessels and nerves. It ends anteriorly in the sclerotic, the termination varying in details in different cases (Elschnig).

The *arachnoid* consists of very delicate white and elastic fibres, containing blood-vessels. It lies nearer the dura than the pia, and is connected with it by denser and more numerous bands, especially near the globe. It ends anteriorly in the inner angle, where the pia passes into the sclera.

The *pial sheath* is thin, consisting of dense connective tissue, with

¹ See PARSONS, 'The Neurology of Vision,' Hodder and Stoughton, London, 1904.

fine elastic fibres. It is closely attached to the nerve, and ends anteriorly by passing for the most part into the sclerotic, but fibres also pass into the choroid.

The *intervaginal space* is normally little more than a potential space. Its anterior extremity varies in shape according to the exact method of termination of the dura in the sclera. Posteriorly it communicates with the subdural space of the brain.

The intra-cranial portion.—The chiasma is made up of nerve-fibres, which are not gathered together into definite bundles separated by bands of neuroglia; nor is the pia mater so closely connected with the surface as in the orbital part of the optic nerve. In the intra-cranial part of the nerve the same condition is found as in the chiasma, but it gradually changes as the foramen opticum is approached, the pia becoming more closely adherent, and sending processes into the nerve, splitting it up into well-differentiated bundles.

The intra-orbital portion.—In the intra-canalicular part the sheaths are closely adherent to each other, the dura is closely adherent to the bone, and the pia to the nerve. The septa are especially numerous in the nerve, and there is a correspondingly rich blood supply. The vena centralis posterior (Kuhnt) runs in the centre of the nerve, collecting the blood from the orbital part, leaving it on the inferior surface, finally opening into the cavernous sinus (Vossius).

As the site of entry of the central retinal vessels (10–20 mm. behind the globe) is approached, the septa diminish somewhat in number. They pass into the nerve from the adherent pial sheath, dividing and anastomosing, thus breaking up the nerve-fibres into bundles which interlace and do not remain as separate, self-contained units. The septa contain many fine elastic fibres. The central vessels enter in a fibrous tissue strand, richly supplied with elastic fibres, at an angle of about 70° – 80° , in the inferior surface. The exact site and mode of entry are not constant. On reaching the axis of the nerve they turn almost at right angles and pass forwards, each giving off one or two branches which pass backwards. At the globe the central vessels anastomose with the circle of Zinn.¹

Beyond the entry of the central vessels the septa again increase in numbers. Here and in the intra-canalicular part there are concentric peripheral septa (Fuchs), and there are also concentric septa around the central vessels. The nerve-fibres are separated from the septa by



FIG. 482.—NORMAL OPTIC NERVE.
Edmunds and Lawford, T. O. S.,
vii. From a child.

¹ See PARSONS, 'The Ocular Circulation,' London, 1903.

a potential lymph space, which can only be demonstrated by injection (Schwalbe).

The nerve-fibres are unusually fine, but vary in size, most being extremely fine. They consist of an axis cylinder and medullary sheath, but have no neurilemma or sheath of Schwann. The axis cylinder and medulla often show varicosities, which are very numerous after inefficient fixation. With Weigert's medullary sheath stain the larger fibres appear as rings in transverse section, whilst the finest fibres are merely points, as if the naked axis cylinder stained. The medullary sheaths cease at the lamina cribrosa, but at slightly different levels in different bundles.

In rare cases the medullary sheaths of the nerve-fibres reappear beyond the lamina cribrosa, and are continued for a short distance as *opaque* or *medullated nerve-fibres* in the retina (v. p. 545). Usually, in these cases a few of the fibres retain their medullary sheaths even whilst they are passing through the lamina cribrosa, but the majority lose them here. Very rarely the opaque fibres may spread out so far as to involve the macula (Hawthorne). In rare cases, too, re-medullation occurs at some distance from the disc, the intervening area being normal (v. Recklinghausen, Caspar, Stephenson, Blaschek, Ulbrich). A transverse band of medullated fibres is normal in the rabbit.

Medullation of sensory nerves occurs late in intra-uterine life and proceeds from the central nervous system towards the periphery. The optic nerve is the last to become medullated (Westphal), and the sheaths do not reach the lamina cribrosa in man until a month or two after birth (E. v. Hippel). Opaque nerve-fibres in the retina are therefore not, strictly speaking, congenital. They have been examined anatomically by Virchow, v. Recklinghausen, Schmidt-Rimpler, Manz, Usher, and others.

The neuroglia consists of cells and fibres interspersed amongst the nerve-fibres. The cell bodies are not normally visible; the nuclei vary in size, shape and staining capacity. The fibres are fine, mostly straight, crossing each other so as to form polygonal meshes in which the nerve-fibres lie. The cells lie partly on the septa, especially the finest ones, and partly amongst the nerve-fibres, especially near the axes of the bundles. Only the chromatin of the nuclei and the fibres are stained by Weigert's neuroglia stain. The cell bodies have been examined in teased preparations (Leber), and by the Golgi method (Greeff); by the latter they are seen to be typical spider cells. The neuroglia has also been examined by a modified Weigert method (Jacoby). Under pathological conditions the cell bodies are often clearly visible.

There is a special glial mantle (v. *infra*) in relation with the peripheral septa, and corpora amylacea (v. *infra*) are often found scattered about.

The intra-bulbar portion.—The opening in the eyeball through which the optic nerve passes varies according to the manner in which the sheaths pass into the sclera and choroid. According to Kuhnt three chief types are found. The commonest is the conical form, in which the canal dwindles from behind forwards, so that the choroidal aperture

is the smallest part. Less commonly the level of the inner scleral lamellæ is the narrowest part, and the walls are either parallel anterior to this, the conical-parallel type, or again expand, the doubly triangular or conical type. According to E. v. Hippel the inner scleral lamellæ may occasionally be the widest part, so that there is an "elbow-like expansion"; since the condition is found in the new-born it is not an acquired anomaly.

The axis of the canal may be antero-posterior, or directed forwards and outwards, the inner opening being displaced outwards; it is much more rarely displaced inwards, so that the axis is directed forwards and inwards. Lange, in a five months' fœtus, observed the nerve pass directly outwards at right angles to the sagittal plane.

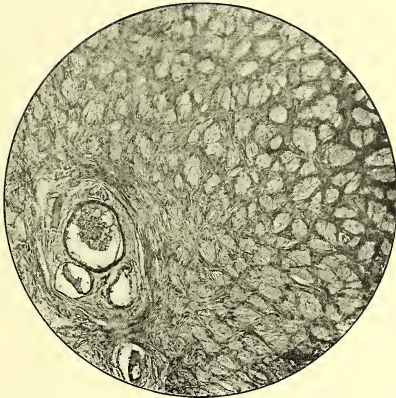


FIG. 483.—ELASTIC TISSUE OF LAMINA CRIBROSA. $\times 60$.

From a specimen by Coats. Transverse section of optic nerve at the lamina cribrosa, stained by Weigert's elastic tissue stain.

The canal is traversed by the lamina cribrosa, a network of fibrous tissue richly supplied with elastic fibres (Fig. 483), derived from the inner half or third of the sclera and the choroid. The choroidal part is much more delicate than the scleral part. It fades off gradually on the anterior surface, whilst the posterior surface is convex and sharply defined. In adults the choroidal chromatophores usually invade the choroidal part for about 0.12 mm., especially in dark people (Berger). The lamina cribrosa is well supplied with blood-vessels derived from the central vessels and the circle of Zinn.

According to Kuhnt, the nerve does not pass immediately into the retina, but is separated from it by a network of neuroglia, or, at any rate, tissue which does not dissolve in trypsin. This "intermediate tissue" varies, but is generally most developed on the nasal side. It

may, perhaps, account for the haziness of the nasal side of the disc on ophthalmoscopic examination in some normal eyes. According to Elschnig, this intermediate tissue, when it exists, is caused by folds of rudimentary retinal tissue. It is generally absent, some layers of the retina passing over the edge of the lamina vitrea and impinging directly on the nerve.

In the conical type of canal the choroid ends in a sharp spur—the choroidal spur, which is sharper on one side when the anterior aperture of the canal is eccentric. The sclera and choroid do not, however, always impinge directly on the nerve, but there is a space which is filled with “limiting tissue,” composed of loose or dense unpigmented connective tissue, rich in elastic fibres (Elschnig). This tissue is vascularised from the choroid, and the elastic fibres are continuous with the supra-capillary elastic network of the choroid. When loose it resembles the choroid, when dense the sclerotic, but it always stains less deeply than the sclerotic with van Gieson. The limiting tissue is covered by the pigment epithelium and lamina vitrea, and sometimes by choroidal capillaries; when strongly developed it passes between the lamina vitrea and the choroidal stroma.

The papilla forms a slight projection into the globe above the level of the surrounding retina; the projection is greater on the nasal side, since more nerve-fibres pass over that side. Neuroglia cells and fibres are fairly evenly distributed amongst the nerve-fibres, and there is a good supply of capillaries.

The physiological cup varies according to the particular form of the scleral canal. The nerve as it passes into the lamina cribrosa becomes diminished in calibre in two manners—by the loss of the medullary sheaths, and by the disappearance of the coarse intra-neural septa. Beyond the lamina cribrosa the condition of the nerve-head depends upon the size of the choroidal aperture. If this is small, there is little or no cup; if large, the nerve-fibres cling to the walls, and the cup is wide and deep; if large and excentric, the cup is drawn over to one side, and this condition may also ensue if the fibrous tissue and neuroglia are more developed on one side than on the other (Elschnig). These conditions and more aberrant ones also may be found in the new-born (E. v. Hippel, Kranz).

The surface of the papilla is covered with a thin membrane, sometimes however several layers thick, derived from the connective tissue around the central vessels; this is pervaded with oval and spindle-shaped nuclei, which rapidly dwindle as the membrane fades off into the membrana limitans interna (Elschnig). This “limiting membrane” is in close relationship with the part of the lamina cribrosa which is derived from the choroid, as is seen best in eyes with a deep physiological cup. When the cup is very deep the membrane is replaced by a mass of connective tissue—“the connective-tissue meniscus” (Kuhnt).

The connective tissue upon the disc is often embryonic in character—hyaline tissue pervaded with branched cells, and frequently containing cystic spaces. Strands containing endothelioid nuclei often stretch into the vitreous; these are remnants of the embryonic vessels

of the vitreous. Remnants of the hyaloid artery are indeed constant up to the thirteenth month (Terrien). Elschnig frequently found an "intercalated tissue" continued from the meniscus around the central vessels backwards as far as or behind the scleral fibres of the lamina cribrosa. This is not of pathological origin (Schoen): the peripheral fibres are arranged concentrically, and have endothelial cells on the surface, whilst the central part is loose, and possesses deeply staining round nuclei as well as the endothelial ones.

KUHNT.—A. f. O., xxv, 3, 1879. BERGER.—A. f. A., xi, 1882. SCHWALBE.—Anat. des Sinnesorgane, Erlangen, 1887. MANZ.—A. f. A., xxix, 1894. E. v. HIPPEL.—A. f. O., xlv, 2, 1898. KRANZ.—Dissertation, Marburg, 1898. KIRIBUCHI.—A. f. A., xxxix, 1899. *ELSCHNIG.—In Magnus, Unterrichtstafeln, Heft 16, 1899; Denkschriften d. k. Akad. d. Wissensch., Math.-naturwissensch. Klasse, lxx, Wien, 1901. *GREEFF.—In G.-S., 1900. LANGE.—A. f. O., li, 2, 1901. SAGAGUCHI.—K. M. f. A., xl, 1902. MOLL.—Hirschberg's Festschrift, 1905. v. RECKLINGHAUSEN.—Virchow's Archiv, xxx. SCHMIDT-RIMPLER.—K. M. f. A., xii, 1874. MANZ.—A. f. A., xxix, 1894. STEPHENSON.—A. f. A., xxxiii, 1896. USHER.—Ophth. Rev., xv, 1896. WESTPHAL.—A. f. Psych., xxix. E. v. HIPPEL.—A. f. O., xlix, 3, 1900. CASPAR.—A. f. A., xli, 1900. BLASCHKE, ULBRICH.—Z. f. A., ix, 1903. MAYERWEG.—A. f. A., xlvj, 1903. GILBERT.—K. M. f. A., xlii, 1904. HAWTHORNE.—Ophthalmoscope, ii, 1904. JACOBY.—K. M. f. A., xliii, 1905.

Artefacts.—It has already been mentioned that the optic nerve fibres often show varicosities, which affect principally the medullary sheaths,

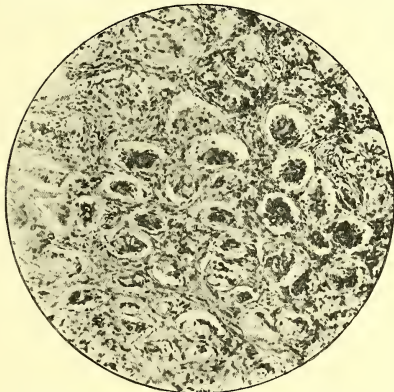


FIG. 484.—ARTEFACTS IN THE OPTIC NERVE. $\times 120$.

From a photograph by Coats. Showing separation of the nerve-bundles from the trabeculae.

but also to some extent the axis cylinders. These varicosities are much increased by deficient fixation and hardening. They may even give rise to bodies resembling corpora amylacea (Ginsberg).

Siegrist described particulate patches of degeneration in the nerve as a common occurrence. Neighbouring patches may fuse, so that a

diffuse degeneration is seen. By Marchi's method broken up masses of fat stain in the manner characteristic of early degeneration, and by Weigert's method fibres devoid of medullary sheaths are demonstrated. Siegrist described the condition at length, and discovered it in very different diseases; he attributed it to the deleterious action of toxins.

The condition is not pathological, but is due to manipulation and inefficient hardening (Elschnig, Fuchs, Wagenmann). It has been exhaustively investigated by Elschnig. Various forms of artefact are easily brought about in the optic nerve, according to this author. There are frequently clefts between the nerve-fibres and the septa, especially near the centre. They may be empty, or nerve-fibres may be present, and they are generally traversed by neuroglia. They are due to dilatation of preformed potential spaces by a so-called "imbedding oedema." The changes described by Siegrist are caused for the most part by injury during excision—crushing between the blades of the scissors, or in freeing from the optic foramen, &c. The fibres and cells often form spiral or concentric whorls—"nerve-fibre convolutions." Elschnig reproduced the appearances even after hardening by crushing normal nerves, and they are always present near the point of section in excisions. When the whole nerve is to be examined it is essential to remove the bony wall of the optic foramen with the nerve, separating it from the nerve only after the hardening process is complete.

Similar artefacts are very common in panophthalmitis (Spühler).

SIEGRIST.—A. f. A., xliv, *Ergänzungsheft*, 1901. ELSCHNIG.—A. f. O., xli, 2, 1895; B. d. o. G., 1902; K. M. f. A., xl, 1902. SPÜHLER.—A. f. O., lvi, i, 1903.

The neuroglial mantle.—Fuchs (1885) described a peripheral atrophy of the optic nerve, concentric with the sheaths. In a zone beneath the pia mater there are no nerve-fibres, but only a neuroglial network, which is loose and open in places, especially near the radial septa, and where the mantle impinges upon the nerve-fibres. In the latter position there are places where the neuroglia is collected into a dense reticulum. Similar "atrophic" bundles are found around the largest nerve bundles, and also apposed to the connective tissue round the central vessels. Fuchs recognised the universality of the phenomenon, and attributed it partly to compression by the blood-vessels and partly to mechanical or chemical deleterious agencies in the lymph.

Samelsohn sought to explain peripheral constriction of the field by Fuch's atrophy. v. Michel first asserted that it was no true atrophy, but a failure in development of the medullary sheaths. Wagenmann stated that it was present in the new-born, and this was confirmed by Kiribuchi, working under Greeff. Kiribuchi also showed that it was due to a neuroglial mantle, similar to that encasing the brain and spinal cord.

The neuroglial mantle is not regular, but forms an irregular cylinder, strongly developed immediately behind the globe. It dwindles posteriorly, and fails altogether in places, to be again strongly developed in the intra-cranial part. Intra-cranially it covers the chiasma and optic tracts. In this feature the olfactory and optic nerves differ from

the other cranial nerves, and further demonstrate their individuality as parts of the central nervous system.

FUCHS.—A. f. O., xxxi, 1, 1885. SAMELSON, v. MICHEL, WAGENMANN.—B. d. o. G., 1892. OTTO.—Dissertation, Berlin, 1893. KIRIBUCHI.—A. f. A., xxxix, 1899. GREEFF.—In G.-S., Lfg. 17, 1900.

The normal blood-vessels.—The histology of the normal central vessels of the retina as they pass through the nerve is of great importance in estimating the nature and amount of pathological change which may occur. The central vessels enter the nerve in the lower and outer quadrant, usually almost directly below, at 10–12 mm. from the globe, with variations from 7–20 mm. The artery is usually, but not always, behind the vein. They carry in with them a mantle of connective tissue derived from the pia. At the entrance two or three branches are given off, generally two arteries and one vein; these divide rapidly in the septa, and end before they reach the lamina cribrosa. As the central vessels turn forwards, almost at right angles, on reaching the middle of the nerve, a large recurrent branch is given off, which passes backwards, keeping to the middle of the nerve, giving off branches as it goes, but disappearing only a short distance from the optic foramen (Vossius).

The central vessels have the following measurements approximately: Diameter of lumen of artery, proximal, 210μ , distal, 170μ ; of vein, proximal, 245μ , distal, 200μ ; thickness of wall of artery, in adult, 32μ , in old age, 37μ ; of vein, in adult, 22μ .

The structure of the artery resembles that of a medium-sized vessel; it is best seen by staining with van Gieson and with Weigert's elastic tissue stain. The lumen is lined with a single layer of endothelium, the long axis of the cell nuclei being parallel with the axis of the vessel. Beneath the endothelium is a subendothelial or intermediate layer, which is not present at birth, but develops with increasing age (see "Senile Degeneration"). It consists of tissue which stains homogeneously with hæmatoxylin or van Gieson, but shows circularly arranged fine elastic fibres with Weigert's elective stain. Outside this is the usual elastic fenestrated membrane or *membrana elastica interna*. The media consists of circularly arranged unstripped muscle-fibres with rod-like nuclei; there is little connective tissue. Then follows an indefinite *membrana elastica externa*, which fades off into the adventitia. This consists of connective tissue with much elastic tissue, arranged in bundles of circular and longitudinal fibres; externally it passes gradually into the connective-tissue sheath.

The vein has an endothelial lining, a thin subendothelial layer, a media with very sparse muscle cells, but many elastic fibres, and a thin adventitia with fine fibres, but little elastic tissue. There is neither *membrana elastica interna* nor *externa*.

CORPORA AMYLACEA

Corpora amylacea, or amyloidea, are a normal constituent of the central nervous system; they are also occasionally found in peripheral

nerves. In the optic nerve they are found principally in the proximal part, at and behind the optic foramen, as well as in the chiasma and tracts. They vary much in numbers in different people and in different animals; thus they are almost constant in the chiasma and tracts of the cat and dog. They also show variations in staining reactions, &c., a fact which emphasises their near relationship to other hyaline deposits in the optic nerve (*v. infra*) and elsewhere.

Corpora amylacea, as they occur in the optic nerve, have the following characteristics. They are round or oval, highly refractile, homogeneous or concentrically laminated bodies of a mean diameter of 15-20 μ . They generally possess a definite capsule, which is smooth or irregular on the surface, and often has processes resembling those



FIG. 485.—CORPUS AMYLACEUM. $\times 200$.

From a photograph by Coats. Corpus amylaceum, in the arachnoid sheath of the optic nerve, infiltrated with calcareous salts.

of the neuroglia cells (Leber). They stain yellow with iodine, violet with iodine and sulphuric or hydrochloric acid; blue with hæmatoxylin; yellow or red with van Gieson. They may take on a metachromatic stain with aniline dyes, *e.g.* pink with methylene blue. They do not stain, or only faintly blue, with Weigert's medullary sheath stain. They do not stain with carmin. From these reactions it will be seen that they do not give characteristic amyloid reactions (*v. Vol. I, p. 101*).

Amylaceous bodies, whilst not infrequently present in normal optic nerves, especially in old people, are commoner in atrophic ones. They lie, not only within the bundles amongst the nerve-fibres, but also at the periphery of the bundles, in the spaces between the bundles and the septa, and in the neuroglial mantle. Hence they are to be found in places where there are no nerve-fibres. Leber was originally of the

opinion that they were derived from the nerve-fibres; later he agreed with Besser and Rindfleisch that they were formed from neuroglia cells, a theory which he substantiated by first demonstrating the processes in teased preparations.

Corpora amylacea in the optic nerve show many points of similarity with those found in the central nervous system, and some minor differences. Redlich found them in the neuroglia of the brain and cord invariably after the fortieth year of age; they are essentially a degeneration of the nuclei of the glial cells. They are not noticeably increased in degenerated brains, or at most in the degenerated parts alone. Siebert investigated hyaline degenerations in general, and came to the conclusion that the amylaceous bodies in the nervous system are formed from myelin. He divided hyaline bodies into two classes, according to staining reactions, with amyloid as a criterion. Corpora versicolorata give a violet or blue colour with halogens—iodine, bromine, chlorine; corpora flava, a yellow, like the surrounding tissues. The former, therefore, give the reactions of amyloid, the latter those of hyalin; the former are never formed directly from cells, and never calcify; the latter are always formed from cells, and often calcify.

Stroebe agreed with the nervous origin of the bodies, and Schuster and Bielschowsky pointed out their resemblance to swollen, broken up axis cylinders. Buchholz also saw the similarity to pieces of axis cylinders which had been taken up by cells, whilst Storch emphasised their extreme resemblance to swollen hyaline neuroglia fibres.

Corpora amylacea in the optic nerve belong to Siebert's corpora flava, whilst those of the central nervous system generally conform to corpora versicolorata. Here, however, exactly as in most other cases of hyaline bodies, the staining reactions vary in different cases, and even in different nodules in the same case. They are inert bodies which are undergoing chemical changes, manifested by different staining reactions (*v. Vol. I, p. 96*; also "*Hyaline Bodies on the Optic Disc,*" *infra*).

LEBER.—A. f. O., xix, 1, 1873; xxv, 1, 1879. REDLICH.—Jahrbücher f. Psychiatrie, 1891. SIEBERT.—Virchow's Archiv, cxxix, 1892. STROEBE.—C. f. allg. Path. u. path. Anat., vi, 1895. SCHUSTER AND BIELSCHOWSKY.—Z. f. klin. Med., xxxiv, 1898. STORCH.—Virchow's Archiv, xlvii, 1899. BUCHHOLZ.—Monatsschrift f. Psych. u. Neurologie, v, 1899.

HYALINE BODIES (DRUSEN)

The presence of hyaline bodies, called by the Germans *Drusenbildungen*, or granular formations, upon the optic disc, is a rare condition.

Ophthalmoscopically, the disc is seen to be swollen, and the first impression is usually that the case is one of optic neuritis. The swelling may amount to 12 D. or 14 D. The vision is often unimpaired. More careful investigation shows that the swelling is due to masses of small, translucent nodules. These are variously distributed; they usually surround the vessels at their exit from the nerve, thus involving only the central parts of the disc; in other cases they are mainly situated at the edge of the disc, which they obscure. They may cover the entire surface and even invade the surrounding retina for a limited

distance, or they may form a ring round the disc, which is itself free from them. Both eyes are usually affected in unequal degree. The eyes are often otherwise healthy, but in many of the cases recorded there has been retinitis pigmentosa. In other cases concurrent disease has probably been fortuitous. The prognosis is good.

H. Müller, in 1858, first described concretions at both optic discs in an almost blind man, *æt.* 75. The nerves were atrophic and the retinae exquisitely tigroid. The concretions, which were calcareous, were in about the position of the lamina cribrosa, and were absent from other parts of the nerve and retina. In spite of the atrophy of the nerve, the level of the disc was raised 0.4 to 0.5 mm. above the level of the choroid.

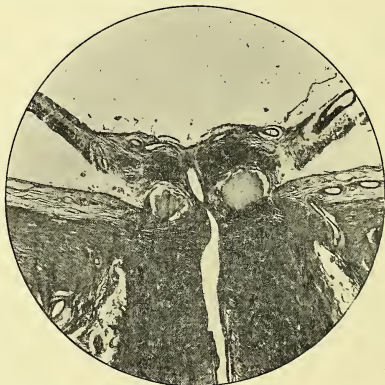


FIG. 486.—HYALINE BODIES AT THE OPTIC DISC. $\times 20$.

From a specimen by de Schweinitz (see T. Amer. O. S., 1892). Concentric lamination of the nodules composing the masses is well seen in the original preparation.

Iwanoff, in 1868, in a paper on optic neuritis, described concretions in the optic nerve, anterior to the lamina cribrosa, in six cases. In the first both eyes were affected, and the vision had been completely intact during life. In the second both eyes were also affected, the patient being insane, with absolute amaurosis. In the remaining four cases only one eye was examined; the eyes were lost from injury or foreign body. In longitudinal sections there were generally two large concretions on each side of the central vessels. These consisted of a great number of quite small, concentrically laminated nodules, resembling amyloid bodies but giving no amyloid reaction. Iwanoff regards them as "*drusige Ablagerungen der Glaslamelle der Aderhaut, welche vom Rande der letzteren aus in den Sehnerven eingedrungen sind.*"

Liebreich was the first to observe the bodies ophthalmoscopically,

as he states in his remarks upon Iwanoff's paper. In such cases, he says, the striking effect of the nerve-fibres is more marked, and bodies are seen in the papilla which reflect the light strongly. They sometimes extend somewhat beyond the choroidal ring. Owing to the strong light reflex they may be easily overlooked. There is often no defect of vision.

Nieden, 1878, described similar appearances in a girl, *æt.* 14 years, with retinitis pigmentosa. There was no consanguinity of parents, and eight other children were normal. Both eyes were affected, the left more than the right.

Jany, in 1879, gave details of a well-marked case with good vision and normal fields. The patient, a woman, *æt.* 37 years, complained of headache and pain in the eyes, which improved under treatment but without alteration in the ophthalmoscopic appearances.

Oeller examined microscopically the eye of a woman, *æt.* 37 years, which had retinitis pigmentosa, and which had been injured when she was 1 year old. There was a mass of laminated concretions lying in the nerve-fibre layer at the outer side of the disc. They had the same consistency as the surrounding tissues, stained faintly with hæmatoxylin, and did not give any amyloid reaction. There were none near the lamina cribrosa, but drops of exudation of all sizes, staining with hæmatoxylin. Oeller combats Iwanoff's theory that the concretions are colloid bodies, and thinks they may be droplets of myelin.

Lawson, in 1883, recorded the first case in England under the title "Syphilitic Choroido-retinitis with Peculiar Growths at the Fundus." In the right eye "upwards and outwards from the disc is a large white translucent patch, composed of very numerous confluent bead-like bodies, looking like the grains of a psammoma (*loc. cit.*, Pl. VIII, fig. 1). . . . The mass projects forwards, as is shown by its overhanging and large retinal vein, and proved also by ophthalmoscopic measurement, the refraction at the most prominent part of the mass being H. 2.5 D., at the neighbouring parts E. The margin of the disc is about half surrounded by a somewhat similar deposit, translucent but not beaded. In the left eye two patches of the confluent beads are present, also near the disc, but the patches are smaller. The larger is seen with + 3 D. There is a diffuse choroido-retinitis." The patches were watched for many weeks but showed no change.

At the same meeting of the Ophthalmological Society, Story showed a case with "anomalous distribution of the retinal arteries" (*loc. cit.*, Pl. IV, fig. 2), probably due to previous blocking of the superior nasal artery. On the right disc were two greyish-white circular spots on the temporal half, rather near the centre (*see plate*). Story mentions a case of Benson's in which similar bodies covered the disc and extended over its edge at several points.

Stood, in 1883, described the clinical characteristics of two cases with (doubtful) optic neuritis. The first was a man, *æt.* 31, with chronic myelitis, paraplegia, and paralysis of sphincters of two years' standing. Both eyes were affected. There was good central vision, with contracted fields and diminution of light sense. The nodules were mostly on the temporal side of the disc and towards the periphery.

There was apparent optic neuritis. Eight years later the nodules were much the same, but the disc was pale, showing signs of optic atrophy. The other case was a girl, $\text{\ae t. 17}$, with hypermetropic astigmatism and convergent strabismus. Both eyes were affected, the nodules occupying a similar position on the temporal sides of the discs, the centres being free. In the left eye there was an anastomosis of two arteries upon the nasal part of the disc; and in the right eye a tag of persistent hyaloid artery projected into the vitreous. Central vision was good; there were contracted fields and diminished light sense. Stood describes optic neuritis, but the evidence is decidedly feeble.

Masselon, in 1884, describes and figures the ophthalmoscopic appearances in the eyes of a man, $\text{\ae t. 57}$, with perfect visual acuity. There are groups of hyaline bodies on both discs, especially in the upper parts, the left disc being covered with them. They are each about the diameter of the large veins, but vary above and below this size. Apart from them and the swelling caused by them, the fundi are quite normal. In a girl, $\text{\ae t. 20}$, with retinitis pigmentosa, $V.=\frac{1}{4}$, and contracted fields, there were hyaline spots at the periphery of the fundus in the neighbourhood of the proliferated pigment epithelium. These were possibly ordinary colloid bodies. The discs were normal.

Schäfer gives an anatomical description of an eye with suppurative irido-choroiditis, in which there were a few laminated concretions, staining faintly, on the lamina cribrosa. The eye was that of a girl, $\text{\ae t. 13}$.

Hirschberg and Birnbacher found *Drusen* on the papilla of a woman, $\text{\ae t. 60}$, who died of cerebral hæmorrhage. There was enormous swelling of the arachnoid sheath of the nerve in this case.

Ancke, in 1885, gave an instructive account of two families with retinitis pigmentosa. In each case three out of five children were affected, and all those affected had *Drusenbildungen* except one, the youngest, $\text{\ae t. 14}$. The ages of the children varied from 16 to 19, and one was of the unpigmented type. In one boy, $\text{\ae t. 16}$, the hyaline bodies had not developed at the age of 14.

Remak describes the ophthalmoscopic appearances in a man, $\text{\ae t. 52}$, with retinitis pigmentosa atypica. The right eye was shrunken, the result of a perforating wound. The lens of the left eye was removed in its capsule for cataract. It was then discovered that there was partial optic atrophy, with hyaline bodies upon the disc. These consisted of five or six large round or oval, bluish-white masses on the inner side of the disc. A few fine vessels passed over them; there were no vessels over the retina. On the inner and outer sides of the retina were a few dense black masses of pigment. Minute investigation was impossible owing to nystagmus. $V.=\text{fingers at } 1\frac{1}{2}\text{ m.}$ It is questionable whether this case belongs to the same category as the others reported.

Wedl and Bock figure in their pathological atlas a section of the nerve-head from the eye of a patient who died of chronic hydrocephalus, $\text{\ae t. 24}$. There are several large calcareous masses, made up of a congeries of small nodules, the smallest being upon the surface.

Gessner, in 1888, described the clinical history and ophthalmoscopic appearances in a case of exophthalmus traumaticus. There were three prominent concretions, resembling mother-of-pearl, on the temporal edge of the disc. $V. = \frac{1}{8}$.

Nieden returned to the subject in 1889, quoting six cases. He gives two good illustrations of the ophthalmoscopic appearances, in one of which the hyaline bodies cover the edges of the disc, whilst in the other they are confined to the central parts. In a man, $\text{æt. } 29$, both eyes were affected, the right worse, the hyaline bodies being confined to the edges of the disc, the centre remaining free. $R. V. = \frac{1}{8}$, $J. 4$; field for blue contracted, probably due to pressure on the nerve-fibres. After adaptation to the pressure, the vision rose to $\frac{1}{15}$, and $J. 1$, but the field for blue remained contracted. The mass reached forward $4 \text{ mm. } (+ 12 \text{ D.})$ into the vitreous. The pressure on the vessels was not sufficient to give rise to pulsation, and on pressing the globe with the finger only the usual venous pulse was elicited. $L. V. = 1$, and $J. 1$. In another case, a man $\text{æt. } 28$, both discs were affected in the centre; in the left the hyaline bodies had spread outwards and reached the edge of the disc in places; in the right they had nowhere extended so far. $R. V. = 1$ and $J. 1$; small corneal abrasion, which rapidly healed; no other disease. $L.$ amblyopic, otherwise healthy. In two of the other cases there had been severe injury to the head, and the *Drusenbildung* was unilateral. It commenced several months after the injuries, and in itself had nothing to do with the failure of sight. One patient, a man $\text{æt. } 24$ years, with hyaline bodies at the edges of the discs, had neurasthenia and other cerebral symptoms. Vision was normal.

Hirschberg and Cirincione, in 1891, published an account of a case of hyaline bodies at the discs associated with a sarcoma of the choroid. They were, therefore, able to examine the eye both ophthalmoscopically and pathologically. The patient was a woman, $\text{æt. } 59$; both discs were affected. $R. V.$ normal; $L. V. = \frac{1}{8}$; field contracted up and in, corresponding to site of a choroidal sarcoma. The appearances in the $R.$ were typical. In the $L.$, after removal, a large mass, 1.5 mm. broad by 0.85 mm. thick, was found upon the lamina cribrosa. It was made up of the usual laminated hyaline bodies, partially calcified. They were cleared up by HCl , evolving gas, but were not dissolved. They were not amyloid.

Gurwitsch describes similar concretions in the eye of a man, $\text{æt. } 34$, who died from chronic interstitial nephritis. The laminated nodules were situated in front of the lamina cribrosa, at the edges of the nerve, near the choroid. They stained strongly with eosin, acid fuchsin, and carmine, not with hæmatoxylin. Small hyaline globules were scattered widely through the nerve in front of the lamina cribrosa, and there were some in the internuclear layer of the retina. Hyaline bodies were absent from the nerve of the other eye.

Purtscher gives a woodcut of the ophthalmoscopic appearances of typical hyaline bodies from the eye of a woman, $\text{æt. } 35$ years. Both eyes were affected. $R. V. = \frac{6}{8}$; $L. V. =$ fingers at 0.3 m.

Terson, in 1892, reviewed the subject in a paper on "*Les verrucosités hyalines de la portion papillaire du nerf optique.*"

de Schweinitz was the first, in 1892, to draw attention to the subject in America. His patient was a man, æt. 45, who was weak-minded, probably as the result of drink; he had been shot in the head twenty years before. In each eye the ophthalmoscopic appearances were closely similar: a slightly prominent papilla, with globular masses forming a circle just within the apparent margin, most prominent above, and capped by glistening particles. R. V. = fingers at 3 feet; L. V. = fingers at 6 feet. Sections show oval masses of concentrically laminated nodules on each side of the central vessels. The whole length of the optic nerves and all the cranial nerves were examined without finding any similar bodies. The nerves were atrophied, but not as a result of the *Drusen*. There were no colloid bodies in the lamina vitrea of the choroid.

Noyes, in discussing de Schweinitz's paper, mentions a young male adult who had had scarlet fever, albuminuria, and neuro-retinitis. Both eyes were affected and remained unchanged for twelve years.

Gifford records the case of a girl, æt. 11, with very extensive affection of the R. disc. V. = doubtful p. l. Papilla and surrounding retina for about half a disc diameter were entirely concealed by a mass of hyaline bodies, the summit of which was 9 D. above the rest of the fundus; below the papilla this mass, after a slight constriction, was continued into another about twice the diameter of the disc. The superior, supero-temporal, and supero-nasal arteries were occluded and formed glistening bands. In the vitreous, mostly in the posterior part, were a number of fine reddish opacities, evidently from comparatively recent hæmorrhages. L. normal. The mass altered considerably during more than two years' watching. The case shows that the prognosis is not always absolutely good, but the loss of vision may have been due to the concurrent vascular disease. In a man, æt. 45, with marked hyaline bodies in both discs, Bright's disease developed a year later, leading to death at the end of another year's interval.

In 1894 de Schweinitz published two cases with similar bodies at the macula.

In the same year Heyl published a case of "albuminoid (?) deposit on the optic disc and retina." The disc showed typical *Drusen*; there was a similar mass at the macula, a large isolated nodule in the retina to the inner side of the disc, and a faint white infiltration elsewhere, with punctate black spots in patches. The other eye had the same condition in less marked degree. The patient had a mitral systolic murmur, and oedema of the legs; no albumen or tube casts.

Sachsaler, in 1898, reported very fully upon a case in a woman, æt. 42. The patient was weak-minded, and died of carcinoma of the stomach. Both discs had a few hyaline bodies at the edges, projecting 4 D. The eyes were otherwise normal. R. V. = $\frac{6}{8}$, L. V. = $\frac{6}{8}$.

We have, therefore, forty-two cases of *Drusenbildungen* more or less fully reported. The cases are really much more numerous than might be expected from the small number recorded, although the condition must be regarded as a rare one. Several cases known to the author have not been reported, and it is probable that the condition is not infrequently overlooked.

The ætiology of the condition is unknown, but an analysis of the cases brings out one or two points of interest. It is noteworthy that seven were cases of *retinitis pigmentosa*; in other cases of this disease it is not uncommon to find similar deposits in the more peripheral parts of the ophthalmoscopic field. Diminution of light- and colour-sense with contraction of fields is a common feature in many of the other cases, and some of these were probably cases of the unpigmented type of *retinitis pigmentosa*; at any rate, they direct attention to a coincident depression of the light-perceiving apparatus, a condition due probably to malnutrition (comparable to the night-blindness of xerosis). The malnutrition in many of the cases seems to be a purely local condition, of which the degenerative changes are the most marked objective sign; in others, those especially associated with nervous disorders, it is more general, and therefore more allied to the cases of xerosis with night-blindness. The other local condition which appears to have some ætiological relationship to the complaint is *injury*. How far this is an unimportant concomitant is not easily determined. It is mentioned in seven or eight of the cases, one of which was also a case of *retinitis pigmentosa*, another one of *enophthalmus traumaticus*; and it was sufficiently striking in Nieden's cases for him to conclude that it may be not infrequently unilateral in cases of injuries to the skull. If due largely to malnutrition, traumatism is quite likely to be an important factor. The association with various *nervous disorders* is recorded in seven or eight of the cases, the nervous condition varying from simple headache or neurasthenia to chronic hydrocephalus and insanity. The important case of de Schweinitz belongs to this group. *Nephritis* (chronic interstitial) was the prominent associated disease in one case, and developed later in another. Association with sarcoma of the choroid and suppurative iridochoroiditis must be regarded as adventitious. There remains a considerable group of cases, probably much larger than the statistics at our disposal would lead us to infer, in which the patients were apparently otherwise normal, both as regards local condition (vision, etc.) and general bodily health.

A general review of the cases leads one to the conclusion that the condition usually commences in early life. Its extreme chronicity, attended in many cases with no defect of vision, accounts for many cases in which the *Drusen* were fully developed in older patients when first examined. The extremely slow development of these bodies is an argument against any relationship with the more acute conditions already referred to, where copious hyaline deposits are regarded as being due to sudden injury, etc. The youngest patient was aged 11 and the oldest 75. Probably sex is of no ætiological importance.

In the great majority of cases both eyes are affected, though often in somewhat unequal degree. Nieden's dictum with regard to unilaterality in skull injuries may be borne in mind; but it is quite likely to be disproved in the future. The probability of such a degenerative change, closely associated with the central retinal vessels, being the outcome of a blood-state, is immensely increased by this prevalence of bilaterality. The prognosis, both for the eyes and for

life, may be considered good, though associated disease must be estimated independently.

There are only two cases recorded in which *Drusen* were diagnosed ophthalmoscopically and the eyes examined pathologically, viz. those of de Schweinitz and of Sachsaler. The anatomical peculiarities of the structures are, however, so characteristic that many other pathological observations are available, and must be considered. In Müller's case there were some large (0.5 mm.) and many small yellowish bodies similar to colloid bodies of the choroid. On treatment with hydrochloric or sulphuric acid the calcareous material was removed, and a concentrically laminated organic substratum remained. They were

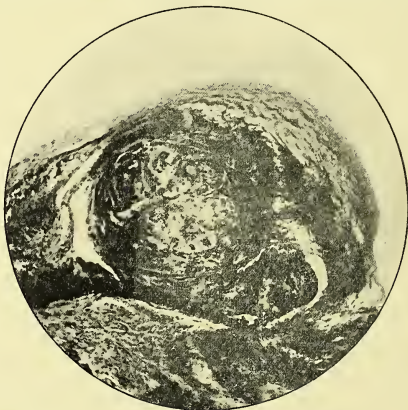


FIG. 487.—"COLLOID BODY" AT THE OPTIC DISC. $\times 55$.

From a specimen by Treacher Collins. This is a true "colloid body" of the choroid, with which it is seen to be in intimate relation. It is covered with dense pigment, and is essentially different from the hyaline bodies in the disc (Fig. 486).

coloured yellow by iodine. They had the same structure in Iwanoff's cases, resembling amyloid bodies. They gave no amyloid reaction, and this observer regarded them, as mentioned above, as colloid bodies. This opinion was accepted by Nieden and Jany as the explanation of their clinical cases. Oeller, after a careful description of the microscopical appearances and reactions in his case, dissented from this view. He found them situated on the outer edge of the disc, extending into the nerve-fibre layer of the retina, and anterior to the choroid, from which they were quite distinct. They offered no resistance to the microtome-knife, and were of the characteristic laminated form, with a crenated contour. The edges did not stain with hæmatoxylin, but the central parts were bluish-red. Iodine reaction was negative. The smallest droplets were found on the lamina cribrosa, and these stained

blue with hæmatoxylin. In a series of sections Oeller was unable to trace any connection with the choroid; moreover, near the disc the lamina vitrea of the choroid had entirely disappeared. He compares them with similar bodies found in the central nervous system, and possibly derived from the myelin of the nerve-sheaths. In Hirschberg and Birnbacher's case the bodies were less developed; they stained deeply with eosin and picrocarmine, and gave no amyloid reaction. Wedl and Bock give no details, but describe their condition as a "Kalkmetastase." Hirschberg, in his communication with Cirincione, investigated the condition more thoroughly. On treatment with hydrochloric acid, the more central concretions gave off a gas and showed their laminated structure; with acetic acid this did not occur, but the peripheral ones cleared up. They gave a yellow colour with iodine, and no amyloid reaction with saffranin or methyl violet. Examination with crossed Nicol prisms showed that they were probably not crystalline (Perles). They were insoluble in water, alcohol, ether, 10 per cent. acetic, 5 per cent. sulphuric, and 10 per cent. potash. Millon's reagent was negative. The authors regarded them as comparable to calcareous nodules in the lungs, and not colloid bodies. Gurwitsch found them in the internuclear layer of the retina, where they could not be derived from the lamina vitrea. He considered them identical with von Recklinghausen's "hyalin," which that author regarded as the precursor of amyloid substance. In de Schweinitz's case the optic nerves and brain were examined, and no similar bodies found there after careful search. In Sachsaler's case the bodies were also present in various layers of the retina near the disc, especially in the outer nuclear layer. A considerable number were found behind the lamina cribrosa, which has not been the case in any other observation. The concretions were submitted to a most exhaustive micro-chemical investigation. The smallest globules stained with eosin; larger ones stained with hæmatoxylin in the centre and eosin at the periphery; the largest stained with neither in the centre, but had an inner zone, staining with hæmatoxylin, and an outer, staining with eosin at the periphery. This author, like Gurwitsch, considers the substance, at any rate in its early stages, to be von Recklinghausen's "hyalin." Previously stated chemical reactions are confirmed. An albuminous constituent is proved by two tests: (1) warming with strong nitric acid gives a yellow colour, which turns orange on addition of ammonia (xanthoproteic reaction); (2) Millon's reagent gives a pink coloration. The concretions turn black with strong sulphuric acid, and parts dissolve with strong potash. Various carmine stains behave like hæmatoxylin, acid fuchsin like eosin. Picrocarmine stains them deeper red the older the concretions are; vesuvin stains them brown, like nuclei. Gram's and Ziehl-Neelson's methods give a negative result. Weigert's fibrin stain gives a deep violet tinge to the younger bodies, but fails to stain the older ones. Russell's method stains the lamina vitrea, etc., green, whilst the concretions become red. Ehrlich's thionin gives a dark violet on a blue ground, or a dark blue on a light blue ground—never green (Kamocki).

Most authors who have not personally investigated the question

adhere to the view that the concretions are colloid bodies (Nieden, Jany, Stood, Masselon, de Wecker, Leber, Ancke, Remak). This view is not borne out either by exact observations or by theoretical considerations. True "colloid bodies" are sometimes found overlapping the edges of the disc, and the appearances which they present microscopically are totally different from those described in all the cases of *Drusen* (Fig. 487). They are exactly like the colloid bodies found elsewhere upon the choroid, and are invariably covered with pigment-epithelial cells derived from the retina. Donders first propounded the theory that these bodies are derived from the retinal pigment epithelium by a colloid metamorphosis of the nuclei. Müller regarded them as outgrowths of the lamina vitrea, and these rival views still hold the field. The former theory has gained ground, and in its latest form the membrane of Bruch itself is regarded as the product of the normal activity of the pigment cells, whilst pathological stimulation of these cells results in the formation of colloid bodies (Treacher Collins). If we accept this view, it is quite impossible for concretions around the central vessels and situated upon the lamina cribrosa to be colloid bodies, seeing that there are no pigment cells there normally, and the specimens show no evidence of their migration there. On the other hypothesis it is necessary to suppose a prolongation of the lamina vitrea across the disc, and anatomical facts are not wanting to show that such may possibly exist (Kuhnt). They can scarcely have survived, however, in Oeller's case, where the membrane of Bruch ceased at a considerable distance from the edge of the nerve. The probability, too, of an inert non-cellular membrane taking on an activity such as is presumed to account for colloid bodies is so remote as to cast great doubt upon the theory.

Further, according to Müller and others, including Oeller, the condition is supposed to be due to obliteration of the chorio-capillaris. This would not account for such structures upon the disc, nor can it be supposed to be present in eyes which are normal apart from the presence of *Drusenbildungen*.

There are other, more general, arguments against the colloid body theory of *Drusen*, which are not subservient to any hypothesis. It is notorious that colloid bodies are the products of extremely chronic irritation, and that they are slow in their development. *Drusen* are found in many young patients, in whom such a condition can scarcely be supposed to have existed for a sufficient length of time. Colloid bodies are, however, supposed to be present in the pigmented areas and elsewhere in many cases of retinitis pigmentosa, but it has not yet been proved that the yellowish spots seen ophthalmoscopically in these cases are true colloid bodies. If they are the strength of this argument is thereby weakened.

The general adhesion to the colloid body theory is doubtless largely accounted for by the indefiniteness of other suggestions. That the concretions should be derived from myelin, as put forward by Oeller, is very unlikely. The corpora amylacea found elsewhere have quite distinctive characteristics, which are not present in *Drusen*; moreover, the great myelin sheaths cease at the lamina cribrosa, and even if we admit

the presence of extremely delicate myelin sheaths, such as probably exist around many so-called non-medullated nerve-fibres, the quantity of myelin present must be very minute. A theory supported by so little evidence scarcely merits further discussion.

Gurwitsch and Sachsaler resort to the very indefinite substance which von Recklinghausen called "hyalin," and which he regarded as the precursor of amyloid material. Now hyaline deposits are quite common in various parts of the eye, and they give the same reactions as von Recklinghausen's "hyalin." On the other hand, in England, amyloid deposits are, at any rate in my limited experience, very rare, although they are undoubtedly seen commonly in the conjunctiva, etc., in other countries, especially Russia. It is probable that "hyalin" is not a definite body at all, and that hyaline deposits are really albuminous exudates undergoing gradual chemical change. This view is supported by the different tints which these deposits assume when treated with stains, so that with methyl violet one gets all gradations from violet to a pinkish tinge, yet not the final clear pink so characteristic of amyloid.

I think it is probable that there are two classes of degenerative deposits found in the eye, viz. (1) those derived from the activity of the epi- or endothelial cells, and (2) exudations. The activity of epithelial cells is represented in the normal condition by the lens capsule and the lamina vitrea of the choroid, that of endothelial cells by Descemet's membrane. Their pathological activity is shown by the formation of a new membrane under a capsular cataract, by "colloid bodies" of the choroid, and by knob-like protrusions and splittings of Descemet's membrane. The second class, exudates, are mainly the coagulated plasma poured out from diseased blood-vessels or deposited by a stagnant lymph-stream, although the death of leucocytes, and even of other tissue-elements, may contribute a share. Whatever be the source, the "exudate" is a dead, inert, proteid mass, and its future history is entirely dependent upon its environment. This varies in an immense variety of ways. It is altered by position, whether in the cornea, the retina, the iris or choroid, etc., whether in close proximity to blood-vessels, etc., and also by the general condition of the individual. In favourable circumstances, *e. g.* near capillaries with a healthy blood-stream, the deposit is rapidly absorbed, probably through the agency of leucocytes. In other circumstances it becomes organised, *i. e.* it affords a rich pabulum to neighbouring connective-tissue cells, which are thereby stimulated to divide and to multiply. In the cornea, in certain conditions, it remains for an indefinite time practically unchanged, when it is known as "hyaline" or "colloid" degeneration of the cornea; but if it is more exposed to desiccation, as near the surface of the cornea, calcareous salts become deposited in it from the blood-plasma. In the choroid, too, it frequently becomes calcified, and is then converted into bone. This process especially commences near the edge of the disc, so that a small ring of bone is formed near the choroid here. So, too, in the retina the exudate may undergo a variety of changes according to very varied circumstances. An example of co-incident fatty and calcareous changes, with deposit of cholesterin, is given on p. 586. It not infrequently becomes organised, or even

calcified, and may then be invaded by osteoblasts derived from the choroid, so that it becomes true bone. This occasionally occurs also at the edge of the disc. An example is shown in Fig. 350, where there is a patch of true bone in the retina at the edge of the disc. The bone is surrounded by multitudes of concentrically laminated bodies, exactly like those found in true *Drusen*. They are quite different from colloid bodies, and one cannot resist the conclusion that they are exudates which have been laid down in layers. The older parts have gradually calcified, and still later ossified. Examples might be multiplied almost indefinitely, but probably one of the best is found in the *Drusenbildungen* upon the optic disc.

H. MÜLLER.—A. f. O., iv, 2, 1858. IWANOFF.—K. M. f. A., vi, 1868. LIEBREICH.—K. M. f. A., vi, 1868. NIEDEN.—C. f. A., ii, 1878. JANY.—C. f. A., iii, 1879. OELLER.—A. f. A., viii, 1879. LAWSON.—T. O. S., iii, 1883. STORY.—T. O. S., iv, 1883. STOOD.—K. M. f. A., xxi, 1883. MASSELOU.—Infiltration vitreuse de la rétine et de la papille, Paris, 1884. DE WECKER ET MASSELOU.—Traité d'Ophtalmoscopie clinique, 2nd ed. SCHÄFER.—C. f. A., viii, 1884. HIRSCHBERG AND BIRNBACHER, ANCKE, REMAK.—C. f. A., ix, 1885. WEDL AND BOCK.—Pathologische Anatomie des Auges, Wien, 1886. GESSNER.—A. f. A., xviii, 1888. NIEDEN.—A. f. A., xx, 1889. HIRSCHBERG AND CIRINCIONE, GURWITSCH, PURTSCHER.—C. f. A., xv, 1891. TERSON.—A. d'O., xii, 1892. DE SCHWEINITZ, NOYES.—T. Am. O. S., 1892. GIFFORD.—A. of O., xxiv, 1895. DE SCHWEINITZ, HEYL.—T. Am. O. S., 1894. SACHSALBER.—B. z. A., xxi, 1898. DE WECKER.—In. G.-S., iv, 1876. LEBER.—In G.-S., v, 1877. DONDERS.—A. f. O., i, 2, 1855. MÜLLER.—A. f. O., ii, 2, 1856. TREACHER COLLINS.—Researches, London 1896. KUHN.—A. f. O., xxv, 3, 1879. STREIFF.—K. M. f. A., xli, 1903, Beilageheft. *PARSONS.—T. O. S., xxiii, 1903. CIRINCIONE.—La Clinica oculistica, 1904. RABITSCH.—K. M. f. A., xliii, 1905.

WOUNDS AND INJURIES

Injuries of the optic nerve in man have seldom been investigated microscopically. v. Michel has recorded two cases in which the nerve has been torn in the neighbourhood of the lamina cribrosa. In the first the nerve was completely divided at the anterior level of the lamina, the space being filled with blood-clot, which had undergone hyaline change in the centre. The anterior part of the nerve was drawn forwards into the eye and the posterior part showed interstitial proliferation. In the second case there were two tears on opposite sides, and both were filled with blood.

The behaviour of the nerve-fibres when the nerve is cut across may be gathered from experiments on animals, and from rare cases in which the nerve has been completely constricted by blood-vessels or tumours. In the former the ends soon become covered with connective tissue, which links them together and invades the spaces between the nerve-fibres and the spaces between the sheaths. The anterior end of the proximal segment may show epithelioid and giant cells (Wagenmann). More experiments are required on this subject, especially some directed towards explaining the peripheral atrophy that takes place.

The second group of cases involve a gradual, and often only partial, obliteration of the nerve. Sachs records a tumour of the pituitary body, which pressed the nerve against the internal carotid and the artery of the corpus callosum, causing complete obliteration on one side. The "pressure atrophy" differed from ordinary secondary atrophy in

the more rapid breaking up of the medullary sheaths, the earlier appearance of wavy fibres—probably naked axis cylinders—and the extensive destruction of neuroglia cells. There was no great proliferation of connective-tissue, such as is found in the traumatic cases. Bernheimer records cases in which sclerosed vessels have almost completely divided the nerve in the intra-canalicular portion.

In all cases of section of the optic nerve the nerve-fibres eventually degenerate, not only centrally, as might be expected from their origin in the ganglion cells of the retina, but also peripherally. Birch-Hirschfeld has shown that the retinal ganglion cells rapidly degenerate after section of the nerve. It may be that the cells and axons are particularly sensitive, so that injury of the axon far from the cell causes shock which leads to atrophy of the cell and the part still attached to it. There is evidence in favour of this view in the analogy of motor-nerves. Thus, if the hypoglossal is cut across the peripheral end shows the ordinary Wallerian degeneration by Marchi's method; if, however, it is forcibly torn out there is also Marchi degeneration in the proximal part. Similarly by the Nissl method, in the first case there is moderate breaking up of the Nissl granules—a degree which is probably capable of repair; in the second case, however, the Nissl granules break up entirely, and it is probable that the cells die (*vide infra*).

Another factor leading to centrifugal degeneration is the efferent fibres which are, undoubtedly, present in the nerve. It is probable that these are more numerous than has hitherto been suspected (Parsons).

Probably the most important factor in many cases is interference with the blood supply, as in cases of optic atrophy following fractures of the base of the skull involving the optic foramen. Here there is not only the local injury and rupture of vessels, but bleeding takes place into the sheaths of the nerve, so that the resulting blood-clot contributes to the atrophy by causing extensive pressure atrophy.

The optic nerve, being part of the central nervous system, does not regenerate. It is true that Stroebe has described the formation of young nerve-fibres in the spinal cord of the rabbit after section, but it is accompanied by rapid proliferation of the interstitial tissue, which prevents functional reunion. Evidence that regeneration occurs in man is lacking.

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INFLAMMATION

Inflammation and œdema of the optic nerve occur in many conditions. The general microscopical features will be considered here; the special forms associated with disease of the central nervous system and other parts of the body will be treated in connection with those diseases.

PAPILLITIS

In papillitis there is considerable swelling, which is chiefly due to œdema. This is greatest and most conspicuous in the "choked disc," a condition which will be treated in detail elsewhere. The swelling causes projection inwards and also increase in diameter; the former leads to ballooning forwards of the choroidal and anterior scleral septa of the lamina cribrosa, and pushes the choroidal spur inwards towards the retina, so that it becomes curved forwards; the latter pushes aside and crumples up the retina, which also participates locally in the œdema. Both directions of swelling lead to partial or complete obliteration of the physiological cup, the connective-tissue meniscus being pushed

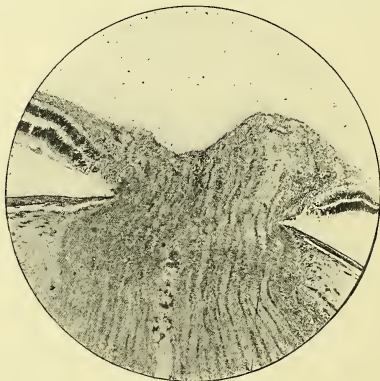


FIG. 488.—OPTIC NEURITIS. $\times 28$.

From the same specimen as Figs. 517-9.

forwards to the surface of the disc. There is little room for swelling in the part of the optic canal traversed by the lamina cribrosa, so that this portion is constricted relatively and throttled—an important factor in the pathogenesis of the condition in many cases. Anterior to the choroidal aperture, especially in the situation of the "intermediate" and "limiting" tissue, the swelling is most marked, so that there is often a tongue-like projection over the edge of the choroidal spur, lying between the choroid and the retina.

In all cases of papillitis there is œdema, less or more pronounced; in true papillitis, as distinguished from "choked disc," there is also inflammatory infiltration. The œdema manifests itself histologically by a general spongy texture, caused by the separation of the normal elements. Fine bright spots or oval or spindle-shaped spaces are seen between the fibres; in hardened sections they are much reduced in

size, owing to the absorption of water, hence the total swelling is greatly reduced also. The spaces are empty, or contain granular coagula, due to the precipitation of proteids by the reagents; they may also contain homogeneous masses of various sizes.

The nerve-fibres are often surprisingly little altered, a fact which accounts for their retention of conductivity and the good vision which is frequently present in the early stages. In severer cases and later stages many are swollen and homogeneous, and they are only with difficulty delimited from the interstitial coagula, which have a similar refractive index. The swelling of the fibres is often irregular, so that they show varicosities. The altered fibres stain deeply with eosin. They break up finally into hyaline masses, some of which form typical "cytoid" bodies (v. p. 578), whilst others resemble corpora amylacea. The cytoid bodies are found chiefly at the edge of the disc, near the surface, and also in the subretinal swelling.

The neuroglia becomes more prominent, partly on account of actual proliferation, chiefly from the œdema, which throws it into relief. The cell-bodies, which are normally invisible, become swollen and show well-marked processes; the cells are also apparently more numerous, since the columns between the nerve-bundles become hypernucleated. The glia fibres are swollen, and can often be stained by specific neuroglia stains (Benda's, Weigert's, Mallory's methods).

Krückmann has carefully investigated the condition of the neuroglial cells in a case of optic neuritis associated with hydrocephalus. The nuclei were very large and clear, with definite nuclear membrane and wide-meshed chromatin network. The smaller and rounder the nuclei, the more diffusely were they stained. The chromatin showed up well, stained brownish, with van Gieson. A few cells were multinuclear, and there were a few mitoses. With Held's neuroglia stain a fine protoplasmic envelope was demonstrated, the neuroglia fibres forming a dense network. Stained with safranin, after fixing in Flemming's solution, the whole of the intra-orbital part of the nerve was found to be strewn with black, osmic-stained clumps of granules. These were mostly massed around the neuroglial nuclei.

The blood-vessels are often sclerosed, a condition which is not always to be attributed entirely to the papillitis, but is frequently due to the underlying cause, *e. g.* nephritis, etc. In all cases of true papillitis there is conspicuous perivascular infiltration with leucocytes, which also invade the connective-tissue meniscus. The vessels are often much contorted, so that the same vessel is cut across several times in the same section; this gives the appearance of proliferation of new vessels, which also occurs to a limited extent. The capillaries are dilated and packed with red corpuscles; they often form distinct networks, with polygonal meshes. The intima of the vessels shows swelling of the endothelial cells, and the walls are frequently swollen and hyaline.

The mesoblastic connective tissue around the vessels and in the meniscus proliferates as the condition progresses. The adventitia becomes thickened by the deposition of new endothelial and other cells. The meniscus increases so as to fill the shrunken physiological

cup, and endothelial membranes are formed, which may extend over the retina. They are, in fact, exactly similar to those often formed on the surface of the retina (v. p. 572). Strands of connective tissue may penetrate for some distance into the vitreous, showing the same characteristics as are found in retinitis proliferans.

When the vessels are much altered, especially in nephritic cases, etc., there may be extravasations of blood; they are usually small.

The infiltration with leucocytes is at first confined to the perivascular connective tissue and the surface of the disc; it is early developed in the latter situation when the neuritis is due to intra-ocular infection—panophthalmitis. In the later stages it becomes general, but is always marked in the sites mentioned. In the later stages, too, many of the cells contain fat globules, forming the so-called fatty granule cells (Fettkörnchenzellen) (*v. infra*). Near the edges scattered pigment may be seen, some free, some in leucocytes; it is partly of retinal origin, partly in many cases hæmorrhagic.

In true papillitis the nerve-trunk is also affected, but in varying degree; an interstitial infiltration is the most marked feature.

In slight cases the nerve may return almost to its normal condition. One such case has been observed anatomically by Ginsberg. The nerve-fibres in the papilla were not altered, but the interstitial tissue was dense and hypernucleated. The vessels showed thickened adventitia, and the new-formed connective tissue on the disc was homogeneous and showed broad hyaline layers with a few scattered long narrow nuclei. In the majority of cases the neuritis goes on to atrophy, with degeneration of the nerve-fibres, increase of the neuroglia and interstitial connective tissue, and disappearance of the œdema and swelling.

INFLAMMATION OF THE NERVE-TRUNK

Inflammation of the trunk of the optic nerve manifests itself histologically by changes—chiefly proliferative—in the interstitial tissues, and by changes—degenerative—in the nerve-fibres. When the former changes are preponderant the condition is called interstitial, when the latter, parenchymatous. Both are invariably present, and both may be due to the same cause, *e. g.* toxins, but there is reason, on clinical as well as on histological grounds, to consider that, as in other parts of the central nervous system, the two types may originate independently. It will be unnecessary in a general survey to consider them separately; special points of difference will be mentioned in treating elsewhere of the individual diseases in which they occur.

The interstitial neuritis may be chiefly peripheral, propagated from the sheaths (*v. infra*, "Perineuritis"), or it may occur primarily around blood-vessels, or it may be general. It is probably generally ushered in by œdema, the fibres being separated from each other by small spaces, which are empty or contain granular coagula. According to Elschnig, increase in the space between the nerve-bundles and the septa is not due to œdema, but to defective hardening, atrophy of nerve-fibres, etc. In "imbedding œdema" the septa are shrunken, not

swollen, and the fibres are not separated from each other. In atrophy of some of the fibres there are often degenerated remnants in the meshes of the neuroglial network, and the latter always pervades the spaces in conspicuous amount.

The septa of the affected areas become densely infiltrated with leucocytes, and there is also an increase in the tissue-cells. This affects the blood-vessels, especially their adventitial sheaths, and also the neuroglia. As regards the former, new vessels are formed, and these carry with them a thin mantle of granulation tissue which rapidly proliferates, with the result that the connective-tissue (pial) septa are greatly thickened. Hence the meshes of the network are encroached upon, and they are further diminished by the subsequent shrinking which the tissue, in common with all granulation tissue, undergoes. Moreover, the fine intra-reticular offshoots of the septa are often most infiltrated in the early stages, and these increase in size and form prominent bands amongst the nerve-fibres. In this manner whole bundles may be snared off, especially at the periphery of the nerve, and cut up



FIG. 489.—OPTIC NEURITIS.

Edmunds and Lawford, T. O. S., vii. From a case of head injury. Note infiltration of trabeculae and distension of intervaginal space. Compare with Fig. 482.

into small islets. The new connective tissue undergoes the usual changes, becoming first fibrillated, later homogeneous, devoid of nuclei and to a large extent of blood-vessels. It is due to these changes in the mesoblastic connective tissue that the nerve-fibres are compressed and distorted, so that they atrophy.

In the early stages of pure interstitial neuritis the nerve-fibres show little change. As they become increasingly compressed and strangled the medullary sheaths break up, forming the characteristic fatty globules which stain by Marchi's method. As the pressure is very unequally distributed, so the degeneration varies in distribution and degree. The peripheral or the central fibres of the bundles may be most affected, but the whole bundle is seldom quite destroyed; even in advanced cases fibres may be seen retaining their sheath, which can be made very evident by Weigert's method.

The neuroglia, too, in pure interstitial neuritis, is chiefly affected secondarily. The cells and fibres are pressed together, so that they appear to be thickened, but probably there is little actual proliferation.

Where the parenchyma is primarily affected, it is the nerve-fibres

and the neuroglia which suffer most. The nerve is usually attacked in an insular manner, though the islets may fuse, leading to partial or complete destruction of extensive areas. It must not be forgotten that the nerve-fibres are conducting elements, so that interference with their insulation (*cf.* Gowers) or loss of their conductivity modifies or abrogates the function of the whole neurone or group of neurones.

The earliest stages of primary atrophy seem to vary with the cause, *e.g.* acute inflammation, tabes, etc. In simple atrophy (q.v.) the axis cylinders are varicose, but this condition is much more pronounced in inflammatory cases, so that they are swollen and greatly thickened, though irregularly. Uthoff found that the medullary sheaths stained more deeply with carmine; they are often thinned, or only stain with Weigert at the periphery. In the later stages they exhibit the same features as in secondary atrophy (q.v.).

The fatty globules derived from the degenerating nerve-fibres are taken up by leucocytes. This occurs in simple secondary atrophy, in which there is little or no evidence of inflammation. In the cases under consideration, where there is much inflammatory infiltration, these fat-containing leucocytes (Fettkörnchenzellen) are a prominent feature, and as they lose all superficial resemblance to leucocytes, they have given rise to considerable discussion. They are not pathognomonic of inflammation, as formerly thought, but their numbers are indicative of the activity of absorption (Bielschowsky). They are usually large, round, bladder-like cells, which may become polygonal by mutual pressure, so that they may resemble epithelioid cells. They have round or irregular nuclei, which stain deeply, so that under a low power they are readily mistaken for an ordinary round-celled infiltration, of which indeed they form a part. If the fat has not been extracted by reagents, the cytoplasm appears granular, and the minute fatty globules stain black with osmic acid and dark blue with Weigert's medullary stain. In ordinary sections the fat is extracted by the alcohol and ether, and the cells appear as unstained holes in the tissues. They are widely distributed in the degenerative nerve—scattered everywhere as isolated cells, grouped in the meshes of the neuroglia from which the nerve-fibres have disappeared, in and upon the septa, in the adventitia and perivascular lymph sheaths.

Neurologists are not agreed as to the origin of the fatty cells; many consider that this varies (Schmaus, Senator, and others). Leucocytes (Schmaus, Ribbert), cells of the adventitia of the vessels (Leyden, Bielschowsky), connective-tissue cells of the pia and endothelial cells of the vessels (Stroebe), and neuroglia cells (Senator, Buchholz, Bielschowsky, Nuel) have all been brought forward as parents of the fatty cells. Their phagocytic character speaks strongly in favour of their leucocytic origin, as also the absence of mitotic figures in the nuclei. The latter fact has been adduced as evidence of connective-tissue or neuroglial origin, on the grounds of the undoubted numerical increase in the mother cells (Ginsberg), but this is well accounted for by increased leucocytosis, and the fact that they are far more numerous in inflammatory conditions than in purely degenerative ones points strongly in the same direction. It has been rightly remarked that the

stimulus to their production need not be necessarily an external irritation, but the mere fact of tissue destruction (Schmaus).

The fatty cells and degeneration products wander into the lymph-channels, from which they slowly disappear, often only after weeks or months; during this period the interstitial infiltration also dwindles or disappears.

The neuroglia is profoundly affected in the parenchymatous types of optic neuritis, for there is evidence of proliferation of the cells as well as thickening of the fibres, only the latter being present in the interstitial types. In the first place the cell bodies become visible, which is not the case normally, and the prolongation of their processes into the fibres become demonstrable. Normally the neuroglial fibres alone stain with specific stains (*e. g.*, Weigert, Benda); this is often so in these cases also, but sometimes the cytoplasm too takes on the stain. The cells then exactly resemble the typical astrocytes (Storch, Bonome, Buchholz). By Golgi's method, Greeff found that the cells were often colossal in size. They formed angular masses, with varicose, bent, or contorted processes. These results can be accepted only in so far as they are confirmed by other less equivocal methods, since the Golgi method is not generally reliable in pathological material. Sourdille attributed the swelling of the cells to œdema, but it has been shown that this tends rather to destruction of the neuroglia and nervous elements than to proliferation (Storch). It is probable that the new cells form fibres, much as connective-tissue cells give rise to fibrous tissue, and as in this case, so here, the cells themselves gradually disappear.

The condition of the septa and interstitial mesoblastic connective tissue in the parenchymatous cases varies. It may be little affected, at any rate in the early stages, and the changes are often confined to irregular areas.

It will have been recognised that the diagnosis of the origin and nature of the disease is often very difficult or even impossible from the histological features alone. The final outcome of the inflammatory processes is an atrophy which differs but little from that caused by primary atrophy of various kinds and ætiology. Some slight guidance may be obtained from emphasising the points of difference in the processes and their results.

There is usually great shrinking of the nerve: this is generally most marked in the interstitial forms of neuritis, owing to the rich production of eminently contractile connective tissue. This leads finally to a shrinkage and distortion of the nerve which is seldom observed in atrophy from other causes; it may, however, be closely simulated (*cf.* "Tabetic Atrophy").

In the earlier stages profuse small-celled infiltration of the septa and meshes is pathognomonic of neuritis as opposed to atrophy. In interstitial neuritis the offshoots of the septa are thickened, whilst in atrophy they are destroyed. This leads in the former case to a dense network of connective tissue, which marks off clearly the intervening meshes, whilst in atrophy only the original septa are thrown into relief, and other parts of the nerve are more or less homogeneous in a bird's eye view.

In the early stages, when the interstitial tissue is relatively little involved, *i. e.* in parenchymatous inflammation, as opposed to atrophy, there is greater swelling of the nerve-fibres, profusion of fatty cells (Fettkörnchenzellen), and increase both in number and size of the neuroglial cells. In the later stages of the same condition it can scarcely be distinguished from primary atrophy. In all cases the general rule is applicable that clinical data must be correlated with anatomical in order to arrive at a well-balanced diagnosis.

LEBER.—A. f. O., xiv, 2, 1868. UTHOFF.—A. f. O., xxxii, 4, 1886; A. f. Psychiatrie u. Nervenheilkunde, xxi, 1890. STROEBE.—C. f. allg. Path. u. Path. Anat., vi, 1895. GREEFF.—A. f. A., ix, 1896. REDLICH, CASSIRER.—C. f. allg. Path. u. path. Anat., ix, 1898. SCHUSTER AND BIELSCHOWSKY.—Z. f. klin. Med., xxxiv, 1898. BUCHHOLZ.—Monatssch. f. Psychiatrie u. Neurol., v, 1899. ELSCHNIG.—Wiener klin. Woch., xi, 1899. STORCH.—Virchow's Archiv, clvii, 1899. MAGER.—Arbeiten a. d. Instit. f. Anat. u. Physiol. d. Centralnervensystems a. d. Wiener Univers., vii, 1900. BONOME.—Virchow's Archiv, clxiii, 1901. BIELSCHOWSKY.—Myelitis u. Sehnervenentzündung, Berlin, 1901. BIRCH-HIRSCHFELD.—A. f. O., lii, 2, 1901. V. MICHEL.—Z. f. A., vii, 1902. KRÜCKMANN.—K. M. f. A., xli, 1903, Beilageheft.

PERINEURITIS

Inflammatory processes may affect chiefly the sheaths of the optic nerve, a condition which is generically termed perineuritis: in consonance

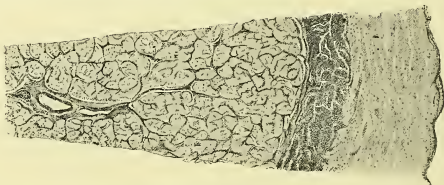


FIG. 490.—PERINEURITIS. $\times 40$.

Edmunds and Lawford, T. O. S., vii. From a case of head injury, fatal in twenty-four hours. Compare with Figs. 482, 489.

with the terminology used in inflammation of the membranes covering the brain, perineuritis is divided into pachymeningitis and leptomeningitis.

Edematous dilatation of the vaginal spaces occurs in a variety of conditions, which will be discussed elsewhere. It often leads to an ampulliform dilatation, an ellipsoidal swelling being produced immediately behind the globe. The dura is then distended and semitransparent; the arachnoid is closely applied to the dura as far as the entrance of the central vessels, after which it generally passes on to the pia. The distension, therefore, affects chiefly the subarachnoid space. A pure hydrops of the vaginal spaces can undoubtedly occur, and commonly accounts for the condition found. It is rare, however, for the manifestations of inflammatory reaction to be entirely absent; when the condition is essentially inflammatory the distension is usually less, and it is more diffuse.

Hæmorrhage into the vaginal spaces may occur from many causes ; when it is associated with hæmorrhage at the base of the brain and increased intra-cranial pressure the dilatation may be typically ampulliform (Uhthoff, v. Michel).

In perineuritis all the sheaths are usually affected, but in varying degree. It may be due to extension from the orbital tissues, or from the membranes of the brain ; rarely it is an isolated phenomenon (v. Michel). The primary cause may be tubercle (Kabsch), syphilis (Uhthoff), purulent meningitis, not only of the base but also of the convexity (v. Michel), cerebral tumours (Elschnig), etc. Owing to the greater or less participation of all three membranes it is not advisable to adhere strongly to the classification into pachy- and leptomeningitis : it is better to divide the cases into purulent and non-purulent. In general, the inflammation is chiefly a leptomeningitis, the dura being relatively little affected owing to its dense structure and lowly organisation ; in this respect it resembles the sclerotic which is derived from it.

In *purulent perineuritis* the vaginal spaces are filled with pus corpuscles. The inner surface of the dura may be so infiltrated and eroded that it is difficult or impossible to delimit it. The outer layers are less infiltrated, except around the vessels. In the less inflamed parts proliferation of the lining endothelium is seen. The arachnoid is imbedded in pus and scarcely recognisable, but the bands passing from it to the dura and pia are often less infiltrated and show up as less deeply stained lines. The pia is densely infiltrated, the small veins are dilated, and minute hæmorrhages are not uncommon. There is often a peripheral infiltration of the nerve-trunk (*vide supra*).

In *simple perineuritis* the corpuscular elements are less numerous. The exuded fluids are rich in albuminous constituents, which coagulate into granular and homogeneous deposits on hardening. Sometimes there is a fibrinous coagulum. The cells consist chiefly of mono- and polymorphonuclear leucocytes, the latter being most abundant in the acute stages ; they are often swollen and degenerated, and may contain fatty globules (Elschnig) ; desquamated endothelial cells are found. The dura shows least change, the inner layers are most infiltrated, and the vessels are dilated and may show perivascular infiltration. Most prominent is the proliferation of the endothelium, which may form nodular protuberances. The arachnoid shows the greatest changes ; it is transformed from a loose network into a dense, highly cellular membrane, with marked endothelial proliferation. In other places it may be rarefied or destroyed, and it is often fused with the dura or pia. The pia shows diffused and nodular infiltration with leucocytes, which may pass along some of the septa into the nerve.

It is important to distinguish between simple œdema of the sheaths, such as is found in nephritis, etc., and true inflammation. In the former condition the arachnoid is swollen and almost homogeneous, but there is little or no infiltration.

In old cases, especially those associated with much proliferation of the fixed cells, the sheaths may become matted together, so that the vaginal spaces are obliterated. This is usually partial, and rarely

extends around the whole circumference, but it interferes so seriously with the nutrition of the nerve that atrophy follows. The new-formed fibrous tissue lies internal to the dura, from which it can be distinguished by the absence of elastic fibres, its fainter staining, and its more definite fibrillation (Elschnig). In other cases there is no obliteration of the spaces, but they are pervaded with a network of connective tissue.

Pachymeningitis chronica.—Under this term v. Michel described a condition in which the endothelium lining the dura is enormously thickened, so as to form a layer visible to the naked eye. It is composed of laminæ of endothelial cells, with whorled groups like those found in psammomata. The arachnoid is often simply drawn inwards, and both this sheath and the pia are little altered. The nerve may show inflammatory atrophy. The condition may be due to tubercle or syphilis, and is often associated with pachymeningitis of the brain.

v. MICHEL.—*Deutsches Archiv f. klin. Med.*, xxii, 1878. SATTLER.—*A. f. O.*, xxiv, 1878. KABSCH.—*Dissertation*, Würzburg, 1882. PRIESTLEY SMITH, SILCOCK.—*T. O. S.*, iv, 1884. UTHOFF.—*A. f. O.*, xxxix, 1, 1893; xl, 1, 1894. ROCHON-DUVIGNEAUD.—*A. d'O.*, xxv, 1895. ELSCHNIG.—*A. f. O.*, xli, 2, 1895. DE LIETO VOLLARO.—*K. M. f. A.*, xli, 1903, Beilageheft.

METASTATIC NEURITIS

Metastatic optic neuritis probably occurs much more commonly than the recorded cases would lead one to expect. v. Michel and Axenfeld have each recorded two cases. v. Michel's first case was a man with epididymitis and endocarditis; both papillæ were hyperæmic, and there was a venous hæmorrhage in each eye. Small patches of infiltration were found in the orbital part of the nerves; each usually had a vessel, filled with granular material, possibly bacteria, in the centre. The second case was a man with pyæmia following a blow on the nose; he had metastatic iridocyclitis. In the left nerve there were three miliary abscesses, the largest in the dura, the others in the nerve. Each consisted of a mass of leucocytes with a minute vessel, filled with cocci in the centre. It is essential in searching for such deposits to cut serial sections (v. Michel).

Axenfeld's first case was a child, æt. 2 months, with pneumococcic meningitis. There were numerous pneumococci in the vaginal spaces, and there was a small (2 mm.) zooglœal mass in a capillary amongst the nerve-fibres. It was surrounded by round cells and fibrin, which also contained pneumococci. In the second case, a marasmic child, æt. 10 days, all the vessels of the eye, lids, orbit, etc., contained streptococci, but these had undoubtedly propagated themselves *post mortem*, a fact of great importance to bear in mind. Whether papillitis can be caused by direct transference of organisms in meningitis from the sheaths is doubtful, since there is no proof that they can pass through the lamina cribrosa (Axenfeld).

It is probable that optic neuritis following infectious diseases is not due to embolism, but to toxins.

v. MICHEL.—*A. f. O.*, xxiii, 2, 1877; *Deutsches Archiv f. klin. Med.*, xxii, 1878; *B. d. o. G.*, 1898; *Z. f. A.*, vii, 1902. AXENFELD.—*A. f. O.*, xl, 3, 1894.

SYPHILIS

The direct effects of syphilis upon the optic nerve have been investigated by Uhthoff. He found the intra-cranial part affected most commonly. It may be attacked here by gumma, or by extension of gummatous infiltration from the meninges, for the neighbourhood of the chiasma is a favourite spot for gummatous meningitis. The nerve may be simply surrounded or an interstitial neuritis may be set up. There is then great infiltration with round cells and granulation tissue.

The intra-canalicular portion may be attacked in the same manner, leading either to descending neuritis or to descending atrophy. The orbital portion may also be attacked directly. Uhthoff found in one case papillitis, retrobulbar perineuritis, and peripheral interstitial neuritis, together with ampulliform dilatation of the sheath. In another case the anterior end of the vaginal space was filled with new connective tissue, whilst the posterior part of the nerve was normal.

The chief histological changes are extreme interstitial proliferation, so that the nervous tissue is destroyed and replaced by granulation tissue, which may later develop into dense fibrous tissue. Baas found excessive endothelial proliferation in addition to ordinary inflammatory changes. From the affection of the vessels he concluded that the nerve may be attacked by extension from the choroid along the perforating ciliary vessels and by way of the anastomosis of the circle of Zinn.

Syphilitic affection of the optic nerve may simulate an intra-ocular tumour, as in Juler's case, and in one which I have examined. In the former the papilla was swollen and the surrounding retina much thickened and partially detached. The optic nerve was twice as thick as normal, being 6 mm. in diameter close behind the globe. Microscopically there was intense leucocytic infiltration of the nerve, retina, and choroid, with some hæmorrhage into the retina, principally in the nerve-fibre layer. The case I examined showed similar microscopic appearances, the head of the nerve being quite necrotic. Though the anatomical examination of these cases showed nothing pathognomonic, the clinical features were such as to scarcely admit of doubt as to the syphilitic nature of the disease.

BARLOW AND NETTLESHIP.—*Trans. Path. Soc.*, xxviii, 1875. FUCHS.—*A. f. O.*, xxx, 3, 1884. HORSTMANN.—*A. f. A.*, xviii, 1889. UHTHOFF.—*A. f. O.*, xxxix, 1, 1893; xl, 1, 1894. NETTLESHIP.—*R. L. O. H. Rep.*, xi, 1896. JULER.—*A. d'O.*, xvii, 1897. BAAS.—*A. f. O.*, xlv, 3, 1898. OTTO.—*A. f. A.*, xliii, 1901. *WAGNER.—*K. M. f. A.*, xli, 1903. STOCK.—*K. M. f. A.*, xliii, 1905.

TUBERCLE

Miliary tubercles in the sheaths and septa of the optic nerve are not infrequently found. Michel described a case of tubercular meningitis with purulent perineuritis and tubercles in the dura and pia. Kabsch, in a similar case, found the vaginal space filled with inflammatory tissue, whilst the pial septa at the periphery of the nerve were studded with miliary tubercles. There were others apparently isolated in the nerve substance, but serial sections showed that these were always

seated on fine vessels. In one case Kabsch found the anterior end of the nerve least affected, whilst in another the lamina cribrosa was especially pervaded with nodules of proliferated endothelium. Only the early stages have for the most part been examined, and caseation has therefore been generally absent.

The optic nerve may be attacked by extension from the eye, the orbit, or the brain. Extension from the eye is not uncommon in cases of choroidal tubercle which are left untreated sufficiently long. Such a case has been reported by Jung. There is general inflammatory in-



FIG. 491.—TUBERCLE OF THE OPTIC NERVE.

From a child who died of general tuberculosis. Coats, R. L. O. H. Rep., xvi, 3.

filtration of the nerve and its sheaths. Giant cells are often present, and occasionally well-formed tubercle systems. There is some proliferative reaction on the part of the neuroglia and connective tissue. The proximal part of the nerve, of course, undergoes secondary atrophy.

Sattler reported a case of extension from the brain. The nerve was transformed into a thick mass of tubercular granulation tissue, caseated in the centre. The papilla and retina also contained tubercles.

Transmission by the lymph-stream is probably the commonest mode of infection, so that the sheaths suffer most frequently and worst. The

inflammatory reaction varies remarkably, so that the vaginal space may be packed with leucocytes, as in purulent perineuritis, or there may be only a few around the tuberculous deposits. All the sheaths may be invaded, but the dura is least vulnerable.

Deutschmann injected pus from a tuberculous knee-joint into the cranial cavities of rabbits. Papillitis and tubercles in the choroid followed. On *post-mortem* examination, besides tubercular meningitis, the optic nerves were found to be in a condition of perineuritis and peripheral neuritis, commencing at the optic foramen. The dural and pial sheaths were studded with tubercles.

Tubercle affecting principally the disc has been rarely observed (O'Sullivan and Story, A. Knapp, Coats; see "Tubercle of the Retina").

DÉMOURS.—*Traité des Maladies des Yeux*, i, 1818. CRUVEILHIER.—*Traité de Path. anat. gén.*, iv, 1862. HJORT.—*K. M. f. A.*, v, 1867. CHIARI.—*Wiener med. Jahrbuch*, 1877. v. MICHEL.—*Deutsches Archiv f. klin. Med.*, xxii, 1878; *Münchener med. Woch.*, 1903. WEISS.—*A. f. O.*, xxiii, 4, 1877. SATTLER.—*A. f. O.*, xxiv, 3, 1878. DEUTSCHMANN.—*A. f. O.*, xxvii, i, 1881. BRAILEY.—*Med. Times and Gaz.*, 1882. WEISSENFELS.—*Meningitis tuberculosa*, Würzburg, 1882. KABSCH.—*Dissertation*, Würzburg, 1882. WAGENMANN.—*A. f. O.*, xxxiv, 4, 1888. CIRINCIONE.—In *Nagel's Jahresbericht*, 1890. JUNG.—*A. f. O.*, xxxvii, 4, 1891. BONGARTZ.—*Nagel's Jahresbericht*, 1891. TREACHER COLLINS.—*R. L. O. H. Rep.*, xlii, 1892. v. HERFF.—*Beiträge zur Kenntniss d. Tuberculose d. Sehnerven*, Würzburg, 1893. BACH.—*A. f. A.*, xxviii, 1894. ELSCHNIG.—*A. f. O.*, xli, 2, 1895. SPALDING.—*T. Am. O. S.*, 1903. *COATS.—*R. L. O. H. Rep.*, xvi, 1905.

LEPROSY

Lie was only able to demonstrate bacilli in one case in the optic nerve, and other observers have generally failed. In this case they were in the middle of the nerve, and there was no inflammatory reaction.

*BORTHERN AND LIE.—*Die Lepra des Auges*, Leipzig, 1899.

DEGENERATIONS

SENILE DEGENERATION

The changes in the optic nerve in old people are chiefly vascular. In young children the endothelium lining the intima of the vessels lies directly upon the elastic lamina. In adults a layer is interposed between them; it may be called the sub-endothelial or intermediate layer. In hæmatoxylin or van Gieson specimens it appears homogeneous, with a few nuclei; specimens stained with Weigert's elastic tissue stain show that it is composed of very fine elastic fibres, running concentrically with the lumen. The layer gradually increases in thickness with age, so that at 60 to 70 a thick elastic layer is present.

Hertel has shown that this is a phenomenon of age, and is independent of true arteriosclerosis. The membrana elastica interna also increases in thickness (Greeff). In the veins no elastica interna is formed, but the elastic tissue in the media increases.

STREIFF.—*Dissertation*, Zürich. HERTEL.—*A. f. O.*, lii, 2, 1901. GREEFF.—In *Orth, Lehrbuch*, Berlin, 1903.

SECONDARY ATROPHY

Most of the optic nerve fibres are afferent fibres, the axons of the retinal ganglion cells. There are also some efferent fibres, the axons of cells which are probably situated in the lateral geniculate body. The ordinary methods have hitherto demonstrated only a few centrifugal fibres, but there are reasons for thinking that they may be more numerous than has been thought.¹ The afferent fibres can be traced and localised in the nerve by suitable lesions of the retina (Dean and Usher, Parsons); similarly section at any part of their course in the nerve leads to degeneration on the proximal side. It is found, however,



FIG. 492.—CUPPING OF OPTIC DISC AND ATROPHY OF NERVE. $\times 10$.

From a man, *æt.* 75, with glaucoma and hypopyon ulcer. The retina is thickened. The deep optic cup is filled with fibrin and organising exudate. The optic nerve is atrophic, and the vaginal space widely dilated.

that after section of the nerve, either by wound, pressure, or destruction by inflammation, the fibres gradually degenerate on the distal side, so that the optic disc becomes atrophic. This is contrary to the general law of Wallerian degeneration, and various theories have been brought forward to account for it.

Sachs, in a case of injury at the chiasma, found that the distal degeneration was most marked near the globe, whilst Elschnig, in a case of compression of the chiasma by a sarcoma, found the degeneration gradually diminish towards the eye. Sachs attributes the distal degeneration to the centrifugal fibres, which he says degenerate more slowly than the centripetal.

¹ See PARSONS, 'The Neurology of Vision,' London, 1904.

Wagenmann, after experimental section of the nerve, found distal atrophy, though the fibres still showed good staining by Weigert's method and the ganglion cells were apparently unaltered. Birch-Hirschfeld, however, using the very delicate Nissl method, was able to prove chromatolysis in the cells, increasing from fifty-five hours after intra-cranial section of the nerve.

There are several possible causes for the distal degeneration, viz. : (1) the efferent fibres; (2) hæmorrhage and interference with the blood and lymph circulation in the nerve; (3) the nature of the injury. The relative importance of these factors must be left to future research. It will probably be found that the centrifugal fibres are more numerous than has been thought. Hæmorrhage into the sheaths and interference with the circulation are undoubtedly important in some cases, *e. g.* fractures of the base of the skull, involving the optic foramen; they will not account for the degeneration in the inflammatory cases. Probably the most important factor is the nature of the injury. It has been found that mere section of a motor nerve, *e. g.* the hypoglossal, causes the ordinary Wallerian degeneration. If, however, the nerve is forcibly torn out, the proximal part shows Marchi degeneration (indirect Wallerian degeneration, van Gehuchten), and the nerve-cells in the nucleus show much greater chromatolysis by Nissl's method than after simple section. It is likely that the highly differentiated ganglion cells of the retina are particularly susceptible to injury, so that less injury than in other parts of the nervous system is sufficient to kill them, thus causing the degeneration in the distal part of the nerve.

The opposition of the cases of Sachs and Elschnig is less striking than might be supposed on superficial consideration. It is quite common, and indeed the rule, for some fibres to degenerate more rapidly and more completely than others after injury, even when there is complete section of the nerve. This is the case with individual fibres (Dimmer) and bundles (Pichler), and is not confined to those of fine or coarse calibre (Dimmer). Sachs found the degeneration confined in one case to bundles which were probably the papillo-macular fibres.

Liebrecht has investigated an interesting series of cases of degeneration from sclerosis of the internal carotid and ophthalmic arteries.

It was long ago pointed out that it is ambiguous to speak of "ascending" and "descending" degeneration, since nerve-fibres degenerate simultaneously, or almost simultaneously, along the whole course beyond the point of section distal to the nerve-cell. It is best to avoid these terms and substitute "proximal" and "distal," using these in the ordinary anatomical sense, and not relative to the cells of origin.

The early histological changes in the medullary sheaths of the nerve-fibres are best investigated by Marchi's method. The broken-down fatty products are then stained black with osmic acid, whilst the normal sheaths remain unstained, being protected by the oxidising agent (potassium bichromate, sodium iodate in the Busch-Marchi method, etc.). Great care must be taken to avoid artefacts, and control preparations must be made by longitudinal section in all cases in which it is desired to trace the course of fibres (Mott, Opin). In the early stages the

sheaths stain normally by Weigert's method, but when the atrophy is complete this method throws the normal fibres into prominent relief. The broken-down medulla slowly passes away by the lymph-channels, in which the fatty globules may be found for weeks and even months. After six months Marchi usually fails to show any stained globules, but complete degeneration of the fibres is not complete for nearly double that period. Many of the globules are taken up by leucocytes, thus giving rise to the fatty leucocytes (*Fettkörnchenzellen*), whilst others are carried along by the lymph-stream.

The finer details of the breaking down of the fibres show that the axis cylinders become varicose and granular in places. Stroebe found clefts in the medullary sheaths, which broke up into cylinders and then

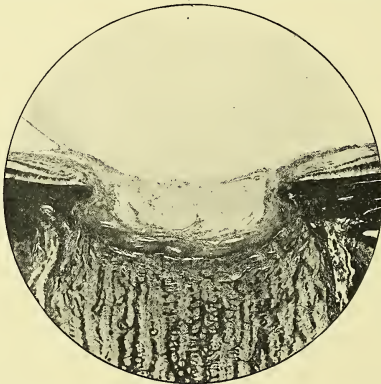


FIG. 493.—GLAUCOMA CUP AND OPTIC ATROPHY. $\times 28$.

From the same specimen as Figs. 182-3, 198, vol. i; 428, 433. Stained by van Gieson's method. Note the fibrous tissue and vessels on the surface of the disc; the cup is filled in with loose connective tissue. The thickened trabeculae (dark) of the atrophic nerve are well seen; the nerve-fibres have degenerated.

assumed the globular form, the axis cylinders soon afterwards breaking across. The later changes in the nerve are described under "Primary Atrophy."

Schnaudigel has described very complete atrophy with the formation of large cavernous spaces in a case of hæmorrhagic glaucoma.

HUTCHINSON, JR.—*T. O. S.*, ix, 1889. WAGENMANN.—*A. f. O.*, xxxvi, 4, 1890. SACHS.—*A. f. A.*, xxvi, 1893. STROEBE.—*C. f. allg. Path. u. path. Anat.*, vi, 1895. HERTEL.—*A. f. O.*, xlv, 2, 1898. DIMMER.—*A. f. O.*, xlviii, 3, 1899. ELSCHNIG.—*Wiener klin. Woch.*, 1900. BIRCH-HIRSCHFELD.—*A. f. O.*, l, 1, 1900. PICHLER.—*Z. f. Heilkunde*, xxi, 1900. LIEBRECHT.—*A. f. A.*, xlv, 1902. VAN GEHUCHTEN.—*Névraxe*, v, 1903. DEAN AND USHER.—*T. O. S.*, xvi, 1896; *Brain*, xxvi, 1903. PARSONS.—*Brain*, xxv, 1902; *The Neurology of Vision*, London, 1904. OPIN.—*A. d'O.*, xxiv, 1904. SCHNAUDIGEL.—*A. f. O.*, lix, 2, 1904.

PRIMARY ATROPHY

Primary atrophy of the papilla.—Primary atrophy of the optic papilla is distinguished ophthalmoscopically from secondary or post-neuritic atrophy by almost complete absence of the new formation of fibrous tissue on the disc. This feature is borne out as a rule on microscopic examination. The papilla is found to be shrunken and flattened, the nerve-fibres have partially or completely disappeared, either over the whole area or over a portion, *e. g.* the temporal side, and the normal tissues are replaced by dense neuroglia, with thin flattened nuclei, representing the compressed glial substratum. There is probably little proliferation in this tissue in most cases, but it is especially well developed in tabetic atrophy.

It is well known that some cases of primary atrophy show considerable development of fibrous tissue on the discs, causing the filling in of the physiological cup which is chiefly associated with post-neuritic atrophy; hence the safe rule that primary atrophy can only with certainty be diagnosed in the absence of such proliferation. So, too, in the microscopical examinations, a considerable excess of fibrous tissue may be found, as in a case of Elschnig's. Here, after blocking of the central artery, the papilla was pervaded with loose fibrous tissue, continuous with the bands of the lamina cribrosa and the perivascular connective tissue. The tissue extended over the edges of the disc into the inner layers of the retina. It is probable that the fundamental cause of the blockage in the artery was responsible for the proliferation (*cf.* "Retinitis Proliferans"); it is unlikely that the degeneration products alone, apart from some additional toxic influence, could produce the result, as in that case one would expect the condition to occur in all primary atrophies.

Primary atrophy of the nerve-trunk.—The histological appearances in the nerve-trunk in cases of primary atrophy of the nerve vary considerably according to the cause. Only a general review of the fundamental changes will be given here, the details associated with individual diseases being left for consideration when these are discussed.

The fundamental factor in all cases is the degeneration of the nerve-fibres, which causes the supporting structures to fall together, thus reducing the bulk of the nerve. In the early stages the meshes of the septal network form large lacunæ, pervaded with fine trabeculæ (Uhthoff). This appearance is not easily distinguished from purely artificial shrinking produced by defective hardening (Elschnig). Fatty granule cells are present, but in far fewer numbers than in post-neuritic atrophy. There is no abnormal infiltration with leucocytes, but Elschnig has found slight perivascular infiltration in the canalicular portion in tabes.

There is never any definite proliferation of the connective tissue. The empty meshes fall together, so that the septa appear to be thickened and more intimately connected. The broad bands are contorted and nodular, owing to their retraction. They are thrown into

prominent relief by van Gieson's stain, whereby they are coloured red, the neuroglial elements being stained yellow. The latter show corresponding changes; they are simply thickened by retraction and compression. There is very little proliferation, though a few astrocytes may be seen. Corpora amylacea are common, especially in the proximal part.

The blood-vessels are dilated and seem to be numerous, though they are really diminished in numbers. They show sclerotic changes, due both to endovasculitis and to perivasculitis. Many are thus obliterated or surrounded by dense fibrous sheaths.

The pial sheath shows apparent thickening, due to the shrinking of the nerve. The arachnoid is shrunken, so that the cells seem to be increased, but there is little more than isolated patches of endothelial proliferation, such as may occur independently of disease. The dura is widely separated from the nerve, which carries with it the other two sheaths; the shrinking of the nerve is less, however, than after inflammatory conditions, though it may be pronounced in tabes.

UHTHOFF.—Arch. f. Psychiatrie u. Neurol., xxi, 1890. ELSCHNIG.—A. f. A., xxiv, 1892. STROEBE.—C. f. allg. Path. u. path. Anat., vi, 1895. STORCH.—Virchow's Archiv, clvii, 1899. BIRCH-HIRSCHFELD.—A. f. O., liii, 1, 1901.

VASCULAR DEGENERATION

A thorough knowledge of the normal structure of the central vessels is essential for an accurate estimate of the degenerative changes which occur in them (*v. p.* 659). In arteriosclerosis the changes which are normal to old age (*v. p.* 685) probably come on earlier, but uniform thickening and development of elastic tissue are not characteristic of the disease. True arteriosclerosis can only be diagnosed with certainty when localised thickenings of a similar nature are found. It is not a common condition, and may be absent when there is profound sclerosis of the other vessels of the body. When present, knobs or bosses are found projecting into the lumen; there is usually only one knob in any given transverse section, but sometimes two or more are present. They are really lens-shaped masses, as can be proved by serial sections. They consist almost entirely of elastic tissue, as is shown by special staining reactions (Weigert, Unna-Tänzer), and they are derived from the intima. The membrana elastica interna, instead of consisting of regular wavy elastic fibres, shows a dense plexus, offshoots of which wander into the intima and media. The media thus shows increase of elastic tissue, but is otherwise normal. Inflammatory changes may be present, shown by slight infiltration, with round cells and unusual richness of nucleated connective tissue.

The inflammatory manifestations are more pronounced in the veins, the adventitial sheaths being densely infiltrated, the medial less, and the intimal least. Bosses of elastic tissue are very rare.

The condition is probably due to chronic toxic irritation. The functions of the retina may remain unimpaired for a prolonged period.

The disease may go on to complete obliteration of the artery

(endarteritis obliterans), very rarely of the vein (Reimar). These affections are merely the final stages of the same process, but the

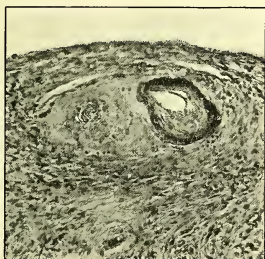


FIG. 494.—VASCULAR DEGENERATION.
× 120.

Coats, R. L. O. H. Rep., xvi. Small artery (right) and vein (left) on papilla, stained by Weigert's elastic tissue stain. Much elastic tissue (dark) in wall of artery; proliferated intima, eccentrically narrowing lumen. Vein has very thick wall, no elastic tissue, and small blood-filled lumen.



FIG. 495.—VASCULAR DEGENERATION.
× 200.

Coats, R. L. O. H. Rep., xvi. Central vein within nerve, stained by Weigert's elastic tissue stain. Many elastic fibres, but no true crenated membrane of Henle. Thickened intima within, with scanty pale nuclei. Lumen lined by fairly even layer of endothelium. Artery to the left.

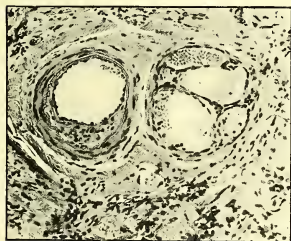


FIG. 496.—VASCULAR DEGENERATION.
× 120.

Coats, R. L. O. H. Rep., xvi. Central vessels in nerve. Artery, to left, shows endarteritis; lumen lined with intact endothelium. Vein, to right, divided into loculi by thin trabeculae lined with endothelium (thrombosis).

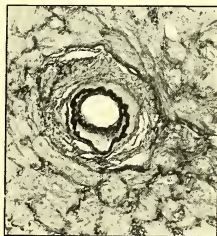


FIG. 497.—VASCULAR DEGENERATION.
× 90.

Coats, R. L. O. H. Rep., xvi. Central artery stained by Weigert. Very thick crenated membrane, within which is a fine feltwork of new-formed elastic fibres.

cellular proliferation is more in evidence: they may, however, also occur as sequelæ of thrombosis or embolism (q. v.).

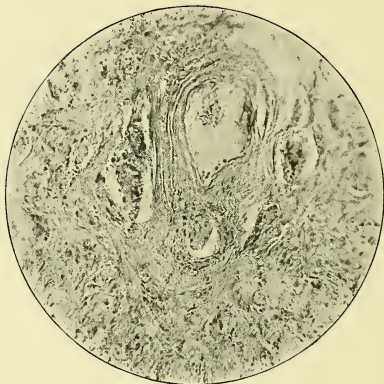


FIG. 498.—THROMBOSIS OF CENTRAL VEIN. $\times 120$.

Coats, T. O. S., xxiv. Central vein in the lamina cribrosa; the lumen is partially occluded by a small mass which has shrunk away from one side. The mass shows some signs of organising. There are no blood-corpuses within the lumen.

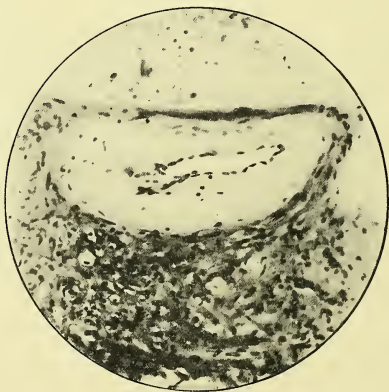


FIG. 499.—FIBROSIS OF A VEIN. $\times 200$.

From a photograph by Coats. The vein is a branch of the central vein and is lying on the edge of a glaucomatous cup, which is seen above. The lumen is concentrically narrowed, the endothelium forming a well-preserved single layer.

The importance of endarteritis obliterans was first emphasised by Heubner (1874); he regarded it as a purely syphilitic product. This view was opposed by Friedländer, though the condition is undoubtedly common in syphilis, as also in nephritis (v. Michel). Hummelsheim and Leber have described a case in diabetes.

Perivascularitis, characterised by dense leucocytic infiltration around the vessels, especially the veins, has already been referred to in considering inflammation of the optic nerve (q. v.).

Hyaline degeneration of the walls of the central vessels, so common in the retinal vessels, is sometimes seen, but it is rare (Greeff). It is often simulated in ordinary sections, but can be distinguished by staining for elastic tissue.

Thrombosis and embolism will be considered elsewhere.

HEUBNER.—Dieluetische Erkrankungen der Hirnarterien, Leipzig, 1874. LORING.—Amer. Jl. of Med. Sc., lxi. NETTLESHIP.—Brit. Med. Jl., 1879. v. MICHEL.—Z. f. A., ii, 1899. REIMAR.—A. f. A., xxxviii, 1899. *HERTEL.—A. f. O., lii, 2, 1901. HUMMELSHHEIM AND LEBER.—A. f. O., lii, 2, 1901. *COATS.—R. L. O. H. Rep., xvi, 1904.

TUMOURS

PRIMARY INTRA-DURAL TUMOURS

The first cases of primary intra-dural tumours of the optic nerve were reported by Wishart (1833) and Middlemore (1838). Goldzieher (1873) first treated the subject of optic nerve tumours apart from orbital tumours, though von Graefe (1864) had already laid down the main diagnostic points. Leber (1877) gave the first attempt at a rational classification. Byers (1901) has collected 102 cases of primary intra-dural tumours.

Age.—Byers has found 85 cases available for exact details as to the age of the patients.

Between	1st and	5th years	.	.	32 cases.
"	5th	" 10th	"	.	20 "
"	10th	" 15th	"	.	15 "
"	15th	" 20th	"	.	9 "
"	20th	" 25th	"	.	5 "
"	30th	" 35th	"	.	3 "
"	60th	" 65th	"	.	1 case.

Hence only 4 cases occurred after the 25th year, so that, like the extra-dural tumours, the condition is essentially one of early life; it is, indeed, probably congenital.

Sex.—The sex is stated in 95 cases; 39 were males and 56 females.

Eye.—In 94 cases the right eye was affected in 42, the left in 52.

Injury.—In 13 cases the growth was attributed to an injury, which in 9 cases was in connection with the head or temporal region, in 3 with the eye itself, whilst in 1 there was a penetrating wound of the orbit.

Febrile disease.—In several cases there is a history of direct relationship with some febrile disease—parotitis, pertussis, measles, influenza, etc.

Exophthalmos is mainly straightforward, thus agreeing with von Graefe's rule for optic nerve tumours in general.

Forwards	14
„ and upwards	1
„ „ and inwards	2
„ „ „ outwards	7
„ and inwards	3
„ „ outwards	3
„ „ downwards	8
„ „ „ and outwards	20
„ „ „ „ inwards	5
Direction not stated	37
No exophthalmos	2

 102

Hence, while proptosis in or about the orbital axis is somewhat characteristic, too much stress is not to be put upon it as a sign of

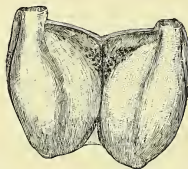


FIG. 500.—TUMOUR OF THE OPTIC NERVE.
After Lawson.

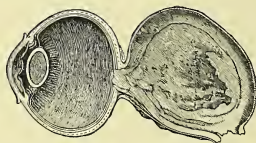


FIG. 501.—INTRA-DURAL TUMOUR.
Rockliffe and Treacher Collins, T. O. S.,
xiii. Macroscopic appearance.

primary tumours of the optic nerve (Byers). The progress of the exophthalmos is almost invariably slow and progressive.

Ophthalmoscopically, out of 82 cases 34 showed optic neuritis, 36 post-neuritic atrophy, and 3 simple atrophy. In Frothingham's and Hulke's cases, which showed no ophthalmoscopic changes, there was half an inch or more of normal nerve in front of the growth. It is possible that not all of the cases called post-neuritic atrophy were really such; some may have been a descending atrophy. There may be progressive hypermetropia, from pressure on the back of the globe (Collins and Marshall); it occurred in 21 of the collected cases.

Macroscopically there is usually a piece of normal or uniformly enlarged optic nerve between the globe and the more or less marked swelling upon the posterior two thirds or three fourths of the nerve; the commonest appearance is that of a pear. Occasionally the greatest development is in the anterior part of the nerve, a pedicle extending

back to the optic foramen (Lawson, Grüning, Taylor, Rockliffe). Often the whole nerve is enlarged, being at its maximum near the middle.

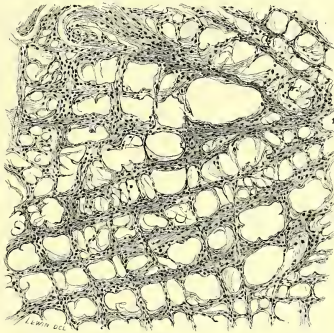


FIG. 502.—INTRA-DURAL TUMOUR.

Rockliffe and Treacher Collins, T. O. S., xiii. Microscopic appearance.



FIG. 503.—INTRA-DURAL TUMOUR OF THE OPTIC NERVE. $\times 100$.

Treacher Collins and Marshall, T. O. S., xx. Transverse section of the growth. From a boy *æ*t. 5.

In two cases a small pedicle of optic nerve existed at both ends of an enlargement centrally situated (Lidell, Goldzieher).

The size varies greatly, and there is often a discrepancy between

it and the symptoms. The tumour may cause scarcely an appreciable swelling (Seggel), or may be as large as a goose-egg (Lidell, Kunachowitch).

The dural sheath forms a capsule, from 0.5 mm. to 1 mm. in

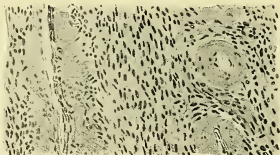


FIG. 504.—INTRA-DURAL TUMOUR OF THE OPTIC NERVE. $\times 100$.
From the same specimen. Longitudinal section.

thickness; it may be loosely applied or thickened and adherent, or thinned and attenuated, rarely to the extent of perforation (Alt, Rockliffe). There may be an outer dense capsule, possibly the thickened fascia between the nerve and the orbital fat (Buller).

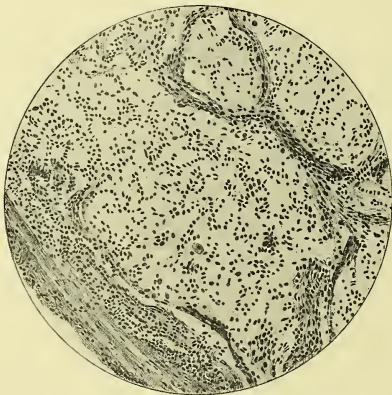


FIG. 505.—INTRA-DURAL TUMOUR OF THE OPTIC NERVE. $\times 100$.
Treacher Collins and Marshall, T. O. S., xx. Transverse section of the growth. From a woman, *æt.* 46.

The core of the enlargement is formed by the nerve and its pial sheath, while between these and the dural sheath, in the distended subdural space, there is always a layer of proliferated cells. The

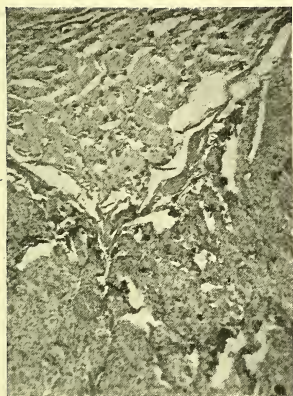
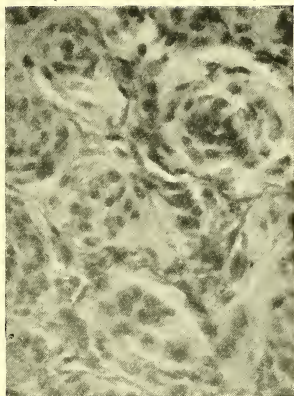
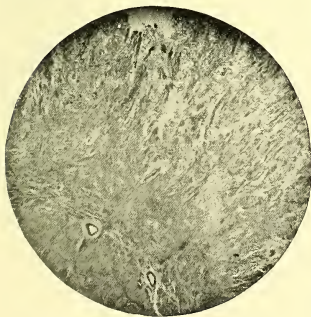


FIG. 506.—INTRA-DURAL TUMOUR.

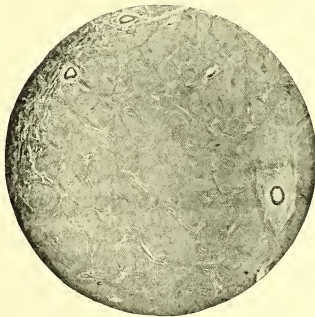
Werner, T. O. S., xxiii. Remains of degenerated nerve shown at apex of triangle above, and tumour tissue below; both lie within the dural sheath.

FIG. 507.—INTRA-DURAL TUMOUR. $\times 400$

Werner, T. O. S., xxiii. From the same specimen. Section through tumour inside nerve sheath, showing whorled arrangement of cell groups.

FIG. 508.—INTRA-DURAL TUMOUR. $\times 20$.

Werner, T. O. S., xxiii. Showing the general appearance of the growth, the stroma of fibrous tissue radiating out from the pial sheath, which is seen to the left and below, together with a portion of the optic nerve.

FIG. 509.—INTRA-DURAL TUMOUR. $\times 20$.

Werner, T. O. S., xxiii. From the same specimen. Transverse section of the optic nerve, showing increase of connective-tissue elements. A portion of the pial sheath is visible to the left, and the central artery to the right.

behaviour of the nerve-core and its surrounding new stratum varies considerably in different cases. The following arrangements are seen in longitudinal sections (Byers) :

(1) The new tissue stratum, mostly developed over the central part of the nerve, ceases to exist at each end, while the nerve proper, normal or nearly so, expands considerably anteriorly and posteriorly in the central region of the swelling (*e.g.* Goldzieher).

(2) The nerve runs unchanged or uniformly enlarged through the whole course of the growth, which occupies, as usual, the subdural space in varying degree (*e.g.* Salzmann, Schiess-Gemuseus, Buller).

(3) The nerve proper gradually increases in size to the optic foramen; the subdural stratum, on the other hand, develops more as the globe is approached (Buller, Byers, Sattler).

(4) The tumour stratum is developed along the whole or posterior part of the nerve, while the nerve proper, normal or nearly so for some distance, expands fan-like and is lost in the growth (*e.g.* Sichel, Salzmann, Vernon, Burnett, Knapp, Willemer).

(5) The nerve proper and subdural stratum developed most anteriorly become normal, or nearly so, at the optic foramen (Tailor, Rockcliffe, Lawson).



FIG. 510.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. Showing the ciliary nerves and ophthalmic artery adherent to the capsule.

In the great majority of cases the excised tumour is incomplete, and must necessarily have been connected with a portion remaining within the cranium. Moreover, while in a large percentage of cases changes, both within and without the nerve proper, go hand in hand, yet in a very limited number of examples this structure may be more or less spared. Though the nerve forms the core, its course through the enlargement is often eccentric; both in longitudinal and transverse section, but especially in the latter, the nerve lies to one side in more or less close contact with the dural sheath, and

the new tissue stratum filling the remaining space has a crescentic shape.

The consistence of the tumours varies from dense and firm to soft and fluctuating; they are nearly always elastic. The consistence frequently varies in different parts of the same growth, especially when there are cystic spaces, which is by no means uncommon. These cavities contain a viscid glairy fluid, which has generally, though probably erroneously, been regarded as mucinous.

The colour is usually yellowish, greyish-red, or reddish-grey; on section, the nerve is distinguishable by its lighter tint and striated appearance. Hæmorrhagic spots are common. Quite frequently the intra-orbital part of the nerve is distinctly increased in length—from a normal 20–30 mm. (Weiss) to as much as 55 mm. (Willemer).

Byers insists upon the frequency of intra-cranial extension in the reports of cases submitted to *post-mortem* examination (10 cases), as

well as of orbital extension of a primary intra-cranial growth. The process is generally limited to the chiasma and the parts extending from it anteriorly. In a very large percentage of cases the primary intra-dural tumours of the optic nerve constitute but a part of a neoplasm more or less widely affecting other structures within the skull.

The reports of the microscopical examinations of these tumours reveal wide differences in nomenclature :

Endothelioma	2
Fibroma	4
Lymphangiectasique fibrome	1
Fibro-myxoma	2
Fibro-nuclear tumour.	1
Fibro-sarcoma	6
Fibro-myxo-sarcoma	4
Glioma	6
Glio-myxoma	1
Glio-myxo-sarcoma	1
Glio-sarcoma	3
Hyperplasia of connective tissue	1
Myxoma	8
Myxo-fibroma	7
Myxo-sarcoma	30
Neuroma	5
Sarcoma	8
„ Elastic neuroglia	1
„ Tubular angio-	1
„ Endothelial	1
„ Angio-myo-	1
Scirrhus carcinoma	1
Not designated	2
„ „ (connective-tissue tumours)	3

100 (Byers).

When the reports are analysed, however, the complexity vanishes to a considerable degree. The term “neuroma,” for example, is used in a general manner for any tumour growing from nerves; since there is no evidence of proliferation of the nervous elements in these cases, and since true neuromata do not occur in the central nervous system, of which the optic nerves form a part, the term is a misnomer and should be eliminated. So, too, the term “glioma” has been used loosely for any connective-tissue growth occurring in nervous structures. It cannot now be considered authentic unless the growth is proved to consist essentially of a neuroglial hyperplasia by the successful application of specific neuroglial stains (Weigert, Benda, Mallory, &c.). In the records of these tumours there is little evidence in favour of specific neuroglial proliferation, though this occurs as a subsidiary phenomenon, whilst there is much in favour of hyperplasia of mesoblastic tissues. There is even more justification for considering that the so-called glio-

sarcomata are mesoblastic: in any case the term is a hybrid monstrosity. The same applies to the glio-myxomata and glio-myxosarcomata. Szokalski's case of scirrhus cancer is admitted by the author to have arisen from the perineurium, and was doubtless an endothelioma (*cf.* Knapp, pp. 710, 715). I therefore agree with Braunschweig, Byers, and others that there is abundance of evidence to show that the growths are all essentially mesoblastic in origin.

Byers points out that intra-dural tumours of the optic nerve do not correspond with any one special type of growth, but that there is constantly represented in one and the same specimen several phases of developing connective tissue. He compares them with the condition found in elephantiasis of the subcutaneous tissues, and uses the term

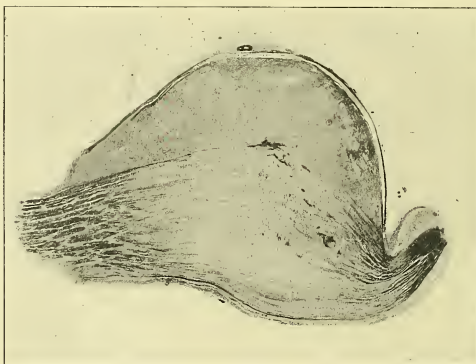


FIG. 511.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. Longitudinal section, stained by Weigert-Pal. Note the distribution of the stained nerve-fibres. There has been some hæmorrhage near the centre of the tumour.

“fibromatosis” to define the general features. There is essentially an overgrowth of white connective tissue which is protean in character. Where the growth is very gradual dense fibrous tissue with few nuclei is formed; where more rapid an almost imperceptible transition to the sarcomatous or myxosarcomatous type is found. These observations agree with those recorded in elephantiasis due to primary obstruction of the lymph-flow. The feature almost invariably described as myxomatous which is so frequently present is in reality a simple œdema, due to lymph stasis. This is proved by local appearances (Schliess-Gemuseus), and still more conclusively by the absence of mucin, as shown by specific tests (Vossius, Salzmann, Delius, and others). The group of cases which show this œdematous condition forms the main

bulk of intra-dural tumours, but there is another well-defined group which belongs to the endotheliomata.

The most characteristic cases of endothelial intra-dural tumours of the optic nerve are those of Alt, Tailor, Kalt, and Byers. The structure exactly resembles that of extra-dural endotheliomata (q.v.). In fact, the extra-dural and the intra-dural tumours of the optic nerve are essentially alike in their slow clinical course, their local malignancy, the absence of metastasis, and their pathogenesis. My views on the last

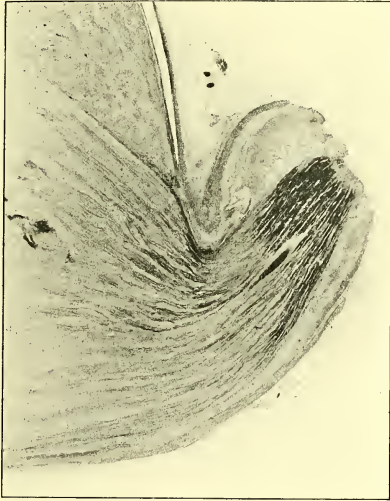


FIG. 512.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. The anterior end of the nerve and tumour (Weigert-Pal). Note the distension of the sheath in front of the tumour, the degeneration in the upper part of the nerve produced by kinking, the process of the pia sheath passing between the upper and the lower portions of the tumour, and the separation of the nerve-bundles by interstitial tissue.

point are stated more fully in discussing the extra-dural tumours; they apply equally to the intra-dural.

WISHART.—Edinburgh Med. and Surg. Jl., xl, 1833. MIDDLEMORE.—London Med. Gaz., xxii, 1838. LIDELL.—New York Jl. of Med., viii, 1860. SZOKALSKI.—Ann. d'Oc., xlv, 1861. V. GRAEFE.—A. f. O., x, 1, 1864; xii, 2, 1866. GOLDZIEHER.—A. f. O., xix, 3, 1873. HOLMES.—A. of O., vi, 1877. BRAILEY.—R. L. O. H. Rep., ix, 1877. ALT.—A. of O., vi, 1878. STRAWBRIDGE.—T. Amer. O. S., 1878. WILLEMER.—A. f. O., xxv, 1, 1879. KNAPP.—T. Amer. O. S., 1879. HIGGENS.—Brit. Med. Jl., 1879. VOSSIUS.—A. f. O., xxviii, 3, 1882; Berlin. klin. Woch., xxii, 1885. AUB.—Amer. Jl. of O., i, 1884. JOHNSON AND

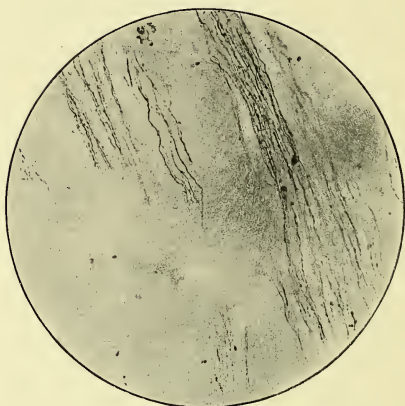


FIG. 513.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. Showing separation of nerve-fibres by interstitial tissue ; the bundle has probably ruptured (Weigert-Pal).



FIG. 514.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. Showing varicose nerve-fibres (Weigert-Pal).



FIG. 515.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. The upper part of the tumour, showing absence of nerve-fibres ; dura and arachnoid are seen above.

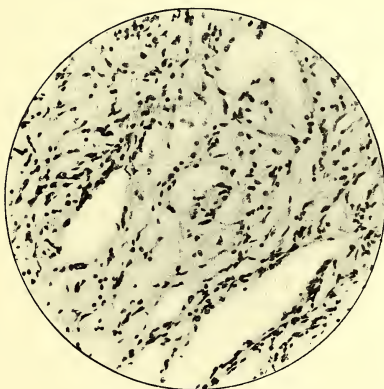


FIG. 516.—INTRA-DURAL TUMOUR.

Mayou, R. L. O. H. Rep., xvi. The upper part of the tumour, showing spaces lined by the tumour-cells.

PRUDDEN.—A. of O., xiv, 1885. LAWSON.—Diseases of the Eye, London, 1885; R. L. O. H. Rep., xii, 1888. SCHIESS-GEMUSEUS.—A. f. O., xxxiv, 3, 1888; Nagel's Jahresbericht, 1889, 1894. ROCKLIFF.—T. O. S., xiii, 1893. TAILOR.—Ann. di Ott., xxiii, 1894. BRAUNTSCHWEIG, SALZMANN.—A. f. O., xxxix, 4, 1893. BURNETT.—T. Amer. O. S., 1894. KALT.—Ann. d'Oc., cxxii, 1899. BULLAR AND MARSHALL.—T. O. S., xix, 1899. A. LAWSON.—T. O. S., xix, 1899. AXENFELD AND BUSCH.—A. f. A., xxxix, 1899. BULLER.—T. Amer. O. S., 1899. COLLINS AND MARSHALL.—T. O. S., xx, 1900. EMANUEL.—A. f. O., liii, 1, 1901. SOURDILLE.—A. d'O., xxiv, 1904. BULLER.—T. Am. O. S., 1902. PAGENSTECHE.—A. f. O., liv, 2, 1902. WERNER.—T. O. S., xxiii, 1903. KURZEZUNGE AND POLLACK.—Z. f. A., x, 1903. MAYOU.—R. L. O. H. Rep., xvi, 2, 1905. *JOCQS.—Des Tumeurs du Nerf optique, Thèse de Paris, 1887. *BYERS.—Studies from the Royal Victoria Hospital, Montreal, 1, 1901. *LAGRANGE.—Tumeurs de l'Œil, ii, 1904.

PRIMARY EXTRA-DURAL TUMOURS

Primary extra-dural tumours of the optic nerve are rare. The following is the description of a characteristic example which came under my notice. It occurred in a girl, æt. 7.

The mass of tissue consists of the whole contents of the orbit,

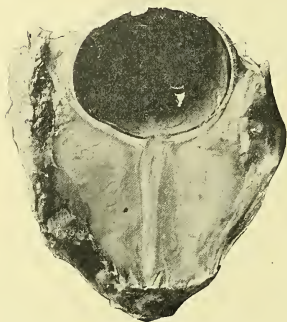


FIG. 517.—EXTRA-DURAL TUMOUR. $\times 1\frac{1}{4}$.

Macroscopic appearances. (See Parsons, T. O. S., xxiii.)

including the globe and eyelids. The greater part consists of a conical mass of dense white growth, moulded to the shape of the orbit. On the inner side it extends forwards to the orbital margin, and constitutes here a hard nodule felt through the skin. The growth anteriorly closely ensheathes the eye, which is not distorted. At the apex the cut end of the optic nerve, surrounded by new growth, is seen, so that the latter probably extends through the optic foramen into the skull cavity. The lids were removed, and the eye and growth, after hardening in 10 per cent. formol, were cut by a sagittal section which divided the nerve longitudinally.

Macroscopic section (Fig. 517).—

The tumour measures 23 mm. from the posterior pole of the eye to cut end of growth. The vertical diameter is 35 mm. in the thickest part, *i. e.* on about a level with the posterior pole of the eye. The horizontal diameter at the same level is about 36 mm. The growth, therefore, practically fills the orbit, extending forwards on the inner side to the orbital margin. It consists of dense white tissue of almost cartilaginous consistence, the peripheral parts being less dense. The anterior surface forms a cup in which the globe lies, the growth being apparently continuous with the sclerotic. The optic nerve is entirely surrounded by, but passes unchanged through, the midst of the tumour, which is evidently continuous with the dural sheath. The cut end of the nerve is surrounded by new

growth, which has also been cut through. It therefore probably extended into the optic foramen, and has not been completely eradicated. The outer surface is smooth, but this is apparently due to the compression exerted upon the orbital walls rather than to any fibrous capsule. The eye is normal except for the swollen disc, which is quite obvious to the naked eye, although the swelling is probably less than before hardening.

Microscopical examination.—The eye is normal except for some retinal congestion with minute hæmorrhages, and marked optic neuritis. The optic disc is much swollen and is hypernucleated, though not more so than the other parts of the nerve (Fig. 488). Apart from a diffuse moderate



FIG. 518.—EXTRA-DURAL TUMOUR. $\times 60$.

From the same specimen. Dura mater to the left, arachnoid (dark), in the middle, and optic nerve to the right.

infiltration with round cells and a distinctly increased number of oval nuclei of endothelial type, the nerve looks normal throughout its length (Fig. 518). The pial sheath is normal. The arachnoid is very evident owing to its great infiltration and the proliferation of its cells. The intervaginal space is much obstructed, the subdural space being absent over large areas owing to the adhesion of the hypertrophied arachnoid. The dural sheath, apart from some infiltration, is normal in its inner layers; peripherally it fades off insensibly into the tumour.

The tumour consists of dense masses of fibrous tissue, mostly hyaline, with a variable number of cells. This tissue is directly continuous with the sclerotic and dural sheath of the optic nerve, Tenon's capsule being unrecognisable. Imbedded in the fibrous tissue are several masses of closely packed, round nuclei, belonging to round cells in the interstices of a definite reticulum. The intervening tissue has a

variable number of cells, and these are mostly of the ordinary spindle-shaped connective-tissue type. Scattered throughout the tissue are many round cells, but there is an absence of leucocytic infiltration. The blood-vessels, which are scanty in the deeper parts, show very well marked endothelial proliferation, and there are many indications of the same process elsewhere. Thus, there are faintly staining, large, oval nuclei, with deeply stained nucleoli, scattered everywhere between the broad hyaline fibres, and these doubtless belong to endothelial cells. There are no definite masses of concentric cells nor any patches of calcification (*corpora arenacea*). At the periphery the growth invades the orbital fat and surrounds the muscles, which it infiltrates without

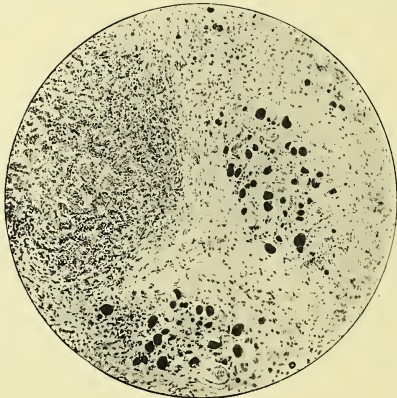


FIG. 519.—EXTRA-DURAL TUMOUR. $\times 60$.

From the same specimen. Showing absorption of orbital fat at the periphery; the dark globules are fat, stained by Sudan iii.

destroying. The fat is gradually absorbed and replaced by new growth, and this process is well seen in sections cut by the freezing microtome, stained by Sudan III¹ and mounted in glycerine (Fig. 519).

The growth belongs clearly to the connective-tissue group, and whilst the embryonic character of the cells is not specially evident, its progressive and infiltrating nature shows that it is sarcomatous. On account of the preponderance of fibrous tissue, it may be called a fibrosarcoma. It is probably of relatively low malignancy, but it is obviously locally malignant.

The relationship of the endothelial cells in the tumour cannot be conclusively decided. As will be seen in the more general discussion on the pathology of these tumours, they are probably nearly all true endotheliomata; and this diagnosis is not inconsistent with the

¹ See PARSONS, R. L. O. H. Rep., xv, 1902.

character of the tumour now described, although it has not yet gone on to the definite formation of groups of concentrically arranged endothelial cells, such as are so typical of the true endotheliomata of the dura mater. In the absence of these bodies it is not surprising that there are no calcareous nodules, as in psammomata.

The exact nature of endotheliomata and their exact position amongst the sarcomata have not yet been settled. In the meantime, we shall be on the safe side in calling the tumour a fibro-sarcoma, with the tentative qualification, endothelioma.

It will be seen from the table that only eighteen cases of undoubted primary extra-dural tumour of the optic nerve have as yet been published.

We may conclude from the paucity of the reported cases that the condition is much rarer than those of the true, or intra-dural, tumours of the optic nerve, which are themselves rare. Of these, 102 cases are collated by Byers (*v. supra*).

Age.—Of the 18 cases, 14 are available for exact details as to the age of the patients. Classifying these in decades, we have:

From birth to 10	.	.	.	.	.	5 cases.
„ 11 „ 20	.	.	.	.	.	4 „
„ 21 „ 30	.	.	.	.	.	1 „
„ 31 „ 40	.	.	.	.	.	1 „
„ 41 „ 50	.	.	.	.	.	2 „
„ 51 „ 60	.	.	.	.	.	0 „
„ 61 „ 70	.	.	.	.	.	1 „

Another patient is reported as being “young.”

The number of cases is too few to be of any value for the determination of percentages, but most of the cases occur before the age of 20. These are the ages at which the patients actually came under observation, and when the proptosis was well developed. If these ages are modified by the less trustworthy details derived from the histories, we obtain the following results as the approximate ages at which the proptosis commenced:

From birth to 10	.	.	.	.	.	7 cases.
„ 11 „ 20	.	.	.	.	.	2 „
„ 21 „ 30	.	.	.	.	.	1 „
„ 31 „ 40	.	.	.	.	.	2 „
„ 41 „ 50	.	.	.	.	.	1 „
„ 51 „ 60	.	.	.	.	.	0 „
„ 61 „ 70	.	.	.	.	.	1 „

Hence, half the cases commenced before the age of 10. The disease is therefore essentially one of early life. The oldest case is 65 (11).¹ It is doubtful whether this case was a tumour of the nerve-sheath at all. It was a small round-celled sarcoma, which did not surround the nerve. From the drawing given in the original, it was adherent to the sheath for only a limited area, and the sheath

¹ The numbers in brackets refer to the table.

was apparently normal. In all probability the tumour originated in other orbital tissues, invading the sheath secondarily. The patient, who was 50 years of age (8), and had had proptosis for six years, was said to have been blind in the eye for eighteen years. Granting this, and eliminating Case 11, all the tumours commenced before the age of 40, and probably considerably earlier.

Sex.—The sex is stated in sixteen cases; ten were males and six females. In the intra-dural tumours there is a preponderance of females.

Eye.—In thirteen cases the right eye was affected in five, the left in eight.

Injury.—Curiously enough, injury is very rarely mentioned in the histories as a cause. This is surprising in consideration of the popular belief that tumours are due to injuries, but is probably explained by the fact that the proptosis would not appeal to the lay mind as being caused by a tumour.

Exophthalmos is usually directly forwards, agreeing with von Graefe's rule for optic nerve tumours in general. In seven of the cases there was some modification, as follows:

Downwards	2
Up and out	1
Down and out	2
Down and in	1
Outwards	1

Hence, as in the case of intra-dural tumours, and perhaps more so, while proptosis in or about the orbital axis is somewhat characteristic, too much stress is not to be put upon it as a sign of primary tumours of the optic nerve.

The progress of the exophthalmos is almost invariably slow and even, usually spreading over months and years. The only rapid case is Case 11, which we have seen reason to doubt as a true tumour of the nerve-sheath. Hence these growths agree in this respect with the intra-dural tumours.

Ophthalmoscopically, in the cases which have been fully reported early in the history of the disease, there has been optic neuritis of the "choked disc" type. In the only case examined pathologically (18) the condition was essentially one of œdema, and was doubtless due to the partial blocking of the intervaginal space. The blocking may have been complete when the parts were *in situ*, and was almost certainly so in the optic foramen. As in cases of early "choked disc" from intra-cranial causes, there was very slender evidence of any true neuritis apart from œdema, there being practically no leucocytic infiltration. Similarly, in this stage, the vision may be normal, as in this case, or but little impaired. In later stages the neuritis is replaced by a post-neuritic atrophy.

During the neuritic stage retinal hæmorrhages have been observed. Other parts of the eye are usually normal until the changes due to lagophthalmia come on, when ulceration of the cornea, etc., supervenes, ending in panophthalmitis and total disorganisation.

In no case has the globe been implicated directly in the growth, nor has progressive hypermetropia from pressure been recorded, as in some cases of intra-dural tumours.

The extra-dural tumours of the optic nerve show a rather remarkable similarity in general type to the intra-dural ones. This is the more remarkable when we remember the very different tissues from which they are respectively supposed to spring. This leads us to doubt how far any of these tumours really spring from the optic nerve itself; in all probability, all, with the exception of the true gliomata, arise from one or other of the nerve-sheaths. In this connection Byers' suggestion of a process of "fibromatosis," comparable to the connection met with in the subcutaneous tissues in elephantiasis, is extremely interesting and luminous. It seems, at any rate, to afford the best working hypothesis which has been brought forward for a very difficult class of case. The slow growth and relatively low malignancy of these growths, combined with their anatomical peculiarities, demand an explanation different from that of the more malignant growths which we are accustomed to classify as sarcomata. In these respects they are more allied to the infective granulomata, but differ from them in being single, usually free from glandular dissemination and from metastasis. The possibility of a local infection should be borne in mind, and the possibility of parasitic influence has more in its favour in these cases than in the case of carci-



FIG. 520.—EXTRA-DURAL TUMOUR.

After Lawson. From a child, æt. 2.



FIG. 521.—EXTRA-DURAL TUMOUR OF THE OPTIC NERVE. $\times 55$.

Brailey, T. O. S., vii. Showing origin of the growth from the dural sheath, with which the fibrous septa (pale) are continuous. In the interspaces are nucleated masses (dark).

nomata and sarcomata. It is not, of course, suggested that they are tuberculous or syphilitic in origin, but it is by no means improbable that many so-called endotheliomata, not only in this situation, but elsewhere, are due to parasitic or toxic irritation. The proliferation of endothelium, so marked in these cases, is an anatomical feature

PRIMARY EXTRA-DURAL TUMOURS

No.	Author.	Age, sex, eye.	Previous history.	Present condition.
1	Scarpa, 1816	Young M. ?	?	Exophthalmos downwards; tumour felt under upper lid
2	Wardrop, 1818	?	?	" Amaurotic eye "
3	Critchett, 1852	28 M. R.	Exophthalmos up and out for fifteen months; no injury	Exophthalmos; preservation of sight; no pain
4	Billroth, 1872	16 M. R.	Exophthalmos eight years; V. impaired nearly as long	Tumour size of fist projecting from R. orbit; bulb atrophied, immovable; orbits widened, especially out; no pain
5	Neumann, 1872	20 M. ?	Migraine six years; exophthalmos three years	Exophthalmos; movements limited upwards; V. = nearly normal
6	Knapp, 1874	40 F. R.	Exophthalmos six months	Exophthalmos down and out; movements limited in all directions, especially up; V. = $\frac{2.0}{100}$, J. 14; intense optic neuritis three years later; V. = $\frac{1.0}{200}$; field normal
7	Savary, 1874	3 M. R.	?	Exophthalmos with chemosis and ecchymoses; hypopyon, synechiæ, yellow exudate in pupillary area; pain; L. photophobia and ciliary injection
8	Dusaussay and Richet, 1875	50 M. L.	No vision in L. for eighteen years, noticed after extraction of a molar; exophthalmos six years, noticed after injury; gradual increase, especially last six months; pain in L. side of head at nights	Considerable exophthalmos, slightly down and in; movements slightly restricted; tumour felt up and in; simple optic atrophy (Galezowski)

OF THE OPTIC NERVE.

Operation.	Pathological anatomy.	Subsequent history and remarks.
Extirpation without enucleation	A knobby tumour the size of a nut composed of "lardaceous or scirrhus tissue," granular, like liver, softened in places; starting from sheath and extending between the levator palpebræ and the superior rectus	"Cure."
Extirpation with enucleation	A tumour of considerable size starting from the "neurilemma"	? Museum specimen.
Extirpation without enucleation	Tumour size of large walnut adherent to sheath, consisting of fibrous tissue with many elongated cells, containing numerous "osseous" particles and a very few small smooth-walled cysts	Suppuration for fifteen days; complete cure, with intact vision.
Extirpation with enucleation	"Psammom-sarcom"; encroached on skull cavity on either side; surrounded atrophied optic nerve	Incomplete removal; severe hæmorrhages at operation; vomiting and unconsciousness a few hours later; death in six days; <i>post mortem</i> , suppurative meningitis.
Extirpation with enucleation	Tumour the size of a nut, $\frac{3}{4}$ " long, surrounding nerve; growing from dura, which forms white line in section; partly compact tissue, partly alveolar; latter like cancer, consisting of fusiform cells with concentric nests, calcified in places; former = large fibres with sarcomatous cells; "psammom"	?
Extirpation without enucleation	Conical tumour, 30 mm. long, 23 mm. thick at base abutting sclera, 27 mm. in vertical diameter; surrounding intact nerve; firm; no cysts; "scirrhus carcinoma," consisting of alveoli with epithelioid cells, concentric nests, and colloid degeneration of stroma; it grew from dural sheath (undoubtedly an endothelioma)	Cure; reported eight months after operation.
Extirpation with enucleation	Pus in a. c.; traces of lens; retina detached; vitreous transformed into a "calcareous mass"; optic nerve enlarged; dura thickened; black gelatinous mass inside sheath (= hæmorrhage); growth = "undoubted myxosarcoma, which appears to have started in the cellular tissue of the sheath"	Rapid recurrence; patient lost sight of.
Extirpation with enucleation	Tumour size of "large chestnut," knobbed, firm; nerve reduced to fibrous cord, indistinguishable inside tumour; very vascular with calcareous nodules, surrounded by concentric layers of cells; "sarcome angiolithique" (endothelioma)	Suppuration; cerebral symptoms; paralysis of R. arm; death in eight days; autopsy, purulent meningitis; small tumour on L. optic nerve intra-cranially.

PRIMARY EXTRA-DURAL TUMOURS

No.	Author.	Age, sex, eye.	Previous history.	Present condition.
9	Chenantaïs, 1879	18½ F. ?	Two and a half to three months' history	—
10	Ewetzki, 1882	14 M. L.	Exophthalmos eight years; slow increase; no pain; loss of vision three years	Exophthalmos down and slightly out; movements much restricted, especially up and in; V. = O; post-neuritic atrophy
11	Lawson, 1882	65 M. L.	Exophthalmos five weeks; rapid increase	Exophthalmos slightly out; immovable; V. = O
12	Peabody, 1883	? M. R.	—	Three weeks' malaise and apathy; meningitis
13	Brailey, 1886	42 F. L.	Exophthalmos eight years; blind seven years	Exophthalmos; movements much restricted; V. = O; hypermetropia + 5 D. (R. + 1 D.); optic disc raised; margin ill-defined, whiter than normal
14	Sutphen, 1889	10 F. L.	Inflamed two years; soon became blind; exophthalmos six months	Globe disorganised; surface furrowed and ulcerated
15	Salzmann, 1890	? ? L.	Injury twenty years before; commenced at inner canthus	Size of fist; only cornea recognisable
16	Lagrange, 1894	5 M. ?	Erysipelas at three months; sloughing of upper lid	Exophthalmos; panophthalmitis
17	A. Lawson, 1899	2 F. L.	Blindness "suspected" three months; exophthalmos a few weeks	Very slight proptosis; movements good: fundus normal, except that the veins were large; three months later marked proptosis, slightly downwards; slight limitation of movements; optic atrophy
18	Parsons, 1902	7 F. L.	Slight injury four months before; treated for "thinness" and headaches one month before	Exophthalmos and ptosis; movements limited in all directions; optic neuritis; small nodule felt at inner side of lower orbital margin

OF THE OPTIC NERVE—*continued*.

Operation.	Pathological anatomy.	Subsequent history and remarks.
Extirpation with enucleation	Size of hen's egg (with globe), firm; eye normal, joined to tumour by loose tissue, except at optic nerve; surrounds nerve, which is normal; alveolar "like some carcinomata"; cells very variable, some large; "névrome médullaire alvéolaire ou sarcome à cellules nerveuses" (probably an endothelioma)	?
Extirpation with enucleation	Ant.-post. = 30 mm.; vert. = 45 mm.; horiz. = 40 mm.; greatest diam. = 55 mm.; loosely attached to sclera; encapsulated; firm, with one calcareous mass; nerve compressed, atrophic; sclera compressed, retina and choroid <i>in situ</i> ; alveolar, with endothelial cells, concentric nests and bands, concretions; endothelioma	Recurrence in three months.
Extirpation with enucleation	Small, round-celled sarcoma	Recurrence, death in three months; metastases in cervical bronchial and abdominal glands, liver, etc.
No operation	Small fibrous tumour, size of half a small French pea; small round-cells between fibres of optic nerve	<i>Post mortem</i> : meningitis; two small abscesses; "sarcomatous tumour developed on the optic nerve and caused meningitis."
Extirpation with enucleation	Tumour "about 1½" in each diameter," surrounding nerve, which "shades off into a fibrous tract"; "fibro-sarcoma starting in outer part of dural sheath"; "whorled arrangement of cells" (probably an endothelioma).	
Extirpation with enucleation	Oval, nodular tumour, 6" broad, 5½" vertically, 2" thick, attached to nerve, which is swollen to double its normal size; small-celled sarcoma	"Cure."
—	Small-celled sarcoma of outer sheath of optic nerve	
Extirpation with enucleation	Ovoid tumour of anterior half of optic nerve; base applied to sclera without being adherent; myxosarcoma of sheath; nerve intact; no true capsule	Cure (reported three months after operation).
Extirpation with enucleation	Tumour, conical, 1" x ¾", surrounding optic nerve for whole length; not encroaching on globe; nerve quite free inside tumour, which is a "myxo-fibroma" of dural sheath	No recurrence fourteen months after operation.
Extirpation with enucleation	Tumour nearly fills orbit; ant.-post. = 23 mm.; vert. = 35 mm.; horiz. = 36 mm.; fibro-sarcoma (? endothelioma)	Probable recurrence (six months after operation).

bridging over the gulf between many chronic inflammatory conditions and these peculiar tumours.

On the hypothesis which I have ventured to bring forward, the condition of "fibromatosis" must be regarded as chiefly secondary in nature, being determined by the obstruction of the normal lymphatic channels. The observations of Vossius, Salzmann, Delius, and others as to the absence of mucin in these cases, I consider to be of prime importance, and it must in future be chemically tested in all the growths in which the so-called mucoid or myxomatous condition is found. If we accept a condition of lymph stasis, it may account for the little tendency to affection of the lymphatic glands. Further, the anatomical disposition of the parts doubtless conduces largely to lymph stasis in the case of orbital growths.

Considering the extra-dural tumours more in detail, the pathological diagnosis is stated in all except the first two. Revising these in the

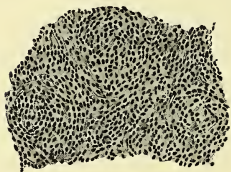


FIG. 522.—EXTRA-DURAL TUMOUR OF THE OPTIC NERVE. $\times 240$.

From the same specimen. Showing part of a nucleated mass; note the whorled arrangement.

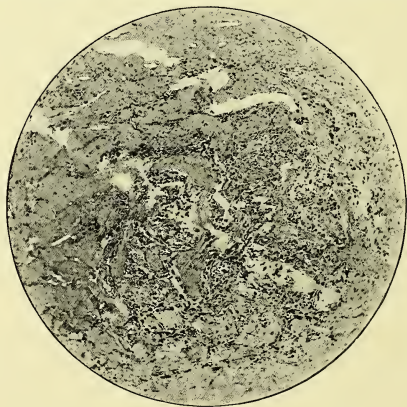


FIG. 523.—OPTIC NERVE INFILTRATED WITH SARCOMA. $\times 55$.

Secondary infiltration of the optic nerve from a sarcoma of the choroid in the neighbourhood of the disc. Bundles of optic nerve-fibres are seen to the left.

light of more recent views, we find that eight may be definitely regarded as endotheliomata (Nos. 3, 4, 5, 6, 8, 9, 10, 13). Of these two (4, 5) are called psammomata, and were doubtless typical tumours of the dura

mater, now commonly regarded as endotheliomata. No. 6 was described as a "scirrhous carcinoma," but the very full description leaves no doubt that it was a psammoma. The descriptions of Nos. 8, 10, and 13 lead to the same diagnosis, though the first and last are called "angiolithic sarcoma" and "fibro-sarcoma" respectively. The reports of Nos. 3 and 9 admit of some doubt as to their true nature, but the presence of "osseous" particles and cysts in the former, and of an alveolar structure "like some carcinomata" in the latter, render the diagnosis of endothelioma probable. To these a ninth case is probably to be added, viz. No. 18. Here, early diagnosis and extirpation probably account for the absence of many of the more characteristic signs; but some doubt must still remain.

In three of the remaining cases the myxomatous degeneration was a prominent symptom. In two of these, judging from the condition of the eyes, the disease had probably existed for a considerable period. In all "fibromatosis" was a prominent feature, although lack of minute detail and the more modern tests render its exact nature doubtful.

No. 12 is to be regarded rather as a curiosity than of any real importance. No history is given; but the extraordinary opinion is stated that a minute "sarcomatous tumour developed on the optic nerve and caused meningitis."

There remain three small-celled sarcomata (Nos. 11, 14, and 15). We have already given some reasons for regarding No. 11 as an orbital tumour involving the optic nerve-sheath secondarily. The lack of detail in the reports of Nos. 14 and 15 render discussion nugatory.

There are, therefore, only twelve cases in which we can be practically certain that the tumours were true primary extra-dural tumours of the optic nerve, and of these nine were almost certainly endotheliomata.

SCARPA.—In Demarquay, *Traité des Tumeurs de l'Orbite*, Paris, 1860; in *Jocqs, *Des Tumeurs du Nerf optique*, Paris, 1887. WARDROP.—*Morbid Anatomy of the Human Eye*, ii, London, 1818. CRITCHETT.—*Med. Times and Gaz.*, v, 1832. BILLROTH.—*Clinical Surgery*, New Sydenham Society, 1881. NEUMANN.—*Arch. f. Heilkunde*, xiii, 1872; *Trans. Internat. Med. Congress* (reported by Knapp), Philadelphia, 1876. KNAPP.—*K. M. f. A.*, xii, 1874; *A. of O.*, iv, 1874. SAVARY.—*Ann. d'Oc.*, lxxii, 1874. DUSAUSSAY.—*Soc. anatomique de Paris*, i, 1875. RICHET.—*Rec. d'O.*, ii, 1875. CHENANTAIS.—*Bull. de la Soc. anat. de Nantes*, 1879; in Jocqs, *loc. cit.* EWETZKI.—*A. f. A.*, xii, 1882. LAWSON.—*R. L. O. H. Rep.*, x, 1882. PEABODY.—*Med. Record*, N.Y., xxiii, 1883. BRAILEV.—*T. O. S.*, vii, 1887. SUTPHEN.—*T. Amer. O. S.*, 1889. SALZMANN.—*Finska lakaresallsk. Handl.*, xxx, 1890; *Annals of Surgery*, ii, 1890; *N. Y. Med. Journ.*, liii. LAGRANGE.—*Journ. de Méd. de Bordeaux*, xxiv, 1894; *Gaz. des. Hôp. de Toulouse*, viii, 1894. ARNOLD LAWSON.—*T. O. S.*, xix, 1899. POCKLEY.—*A. of O.*, xxxi, 1902. *PARSONS.—*T. O. S.*, xxiii, 1903. FRANCKE AND DELBANCO.—*A. f. O.*, lix, 3, 1904.

CHAPTER XII

THE ORBIT

CYSTS

CYSTS of the orbit may be divided into (1) congenital, and (2) acquired. Congenital cysts connected with the globe will be considered elsewhere.

Congenital cysts include (1) dermoid and teratoid cysts; (2) inclusion cysts, meningocele, encephalocele, hydrencephalocele.

Acquired cysts include (1) implantation cysts; (2) serous cysts; (3) parasitic cysts (*a*) hydatid cysts; (*b*) cysticercus cysts.

*LAGRANGE.—*Tumeurs de l'Œil*, ii, Paris, 1904.

CONGENITAL CYSTS

Dermoid and teratoid cysts.—Dermoid cysts of the orbit are relatively common, and early attracted attention. They were first described as melicerides, steatomata, and atheromatous cysts, the earliest reported being the meliceris of Pierre de Marchetis (1640); they were first called dermoids by Lebert (1852). Barnes described a teratoid cyst containing a tooth, Lawrence two cysts containing hairs.

Dermoid cysts of the orbit and its vicinity have often been confused with sebaceous cysts, so that statistics as to their site, etc., are unreliable. True dermoid cysts are invariably congenital. They usually occur at the inner or outer angles, manifesting themselves as rounded tumours under the skin; they also occur in other situations. They vary in size from that of a pea to that of a large orange; like other dermoids, they are liable to take on rapid growth at puberty. Weigert described a teratoma which completely filled the orbit. They frequently extend much more deeply into the orbit than is suspected before operation. They are originally situated outside the cone of muscles, but they often undergo pathological changes due to pressure, inflammation, etc., whereby they contract adhesions to the bones, muscles, and optic nerve. They are commonly orbital from the beginning, but they may also invade the orbit secondarily (Spencer Watson, de Lapersonne).

Para-orbital cysts are frequently seen, usually situated at the outer

or inner extremity of the eyebrow, sometimes extending on to the temple. They are not adherent to the skin, which moves freely over them, but they are generally adherent to the bone, or, if not, there is often a depression in the bone. This depression varies greatly in extent, and may be such that the cyst is in contact with the dura mater. They differ from ordinary sebaceous cysts and from congenital serous cysts in having a thicker wall, as can often be made out by palpation. They are almost invariably opaque, but may rarely be transparent like oily sebaceous and congenital serous cysts (Vassaux and Broca).

The essential histological feature of dermoid cysts is their epithelial lining. This resembles epidermis, but is frequently very atrophic and variable in thickness (Fig. 524). It may be absent in places, but this is always a secondary phenomenon. The wall of the cyst usually

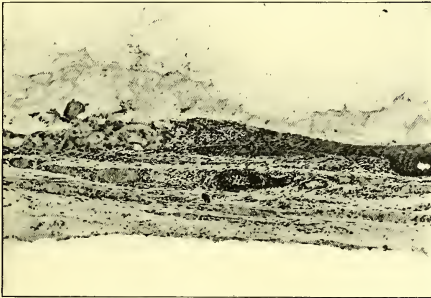


FIG. 524.—DERMOID CYST. $\times 60$.

The wall is lined with stratified epithelium, which, towards the left, is being destroyed and desquamated by the invasion of granulation tissue containing giant cells. The sebaceous contents of the cyst are seen above.

contains other dermal structures—hairs, sebaceous glands, and less commonly sweat-glands. Gradations are met with to the fully developed teratoid growth, containing teeth, muscle, etc.

Mitvalsky divides the dermoid cysts into three groups: (1) with hair-follicles, sebaceous and sudoriparous glands in their walls; (2) with only sweat-glands; (3) with a simple epithelial lining. The last-named are very rare, and may be due to incomplete examination.

The epithelium may be well developed, like epidermis, with papillæ. More commonly, or over the greater part of the surface, it is rudimentary, and composed of one or two layers of flattened, ill-formed cells. The cysts are generally unilocular, but may be multilocular, probably by secondary adhesions. There are sometimes polypoid projections into the cavity, due to inflammatory hyperplasia of the wall. More extensive erosions, etc., may lead to plication of the wall (Mitvalsky).

The hair-follicles and hairs vary with the epithelium ; if this is well developed, they are large and normal in appearance. The younger the individual, the more regular the arrangement of the constituents of the wall. As the secretions of the glands increase, the cyst becomes distended, the wall is compressed and thinned, the hairs are forced into an oblique direction, and their follicles degenerate.

Similarly, the size and development of the sebaceous and sweat-glands are largely dependent on the degree of distension of the cyst. They may be numerous and well-developed (Fig. 525), or scanty—usually arranged in groups—and ill-formed. Distension of the cyst and external pressure may lead to blockage of the ducts. In this

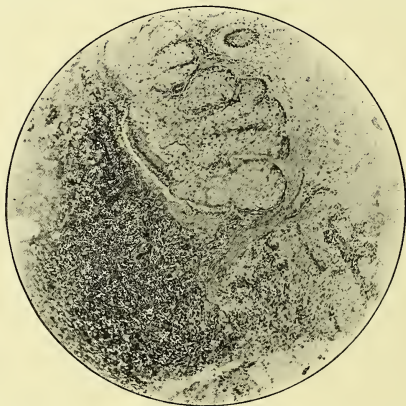


FIG. 525.—DERMOID CYST. $\times 55$.

From a girl, *æt.* 18. Incompletely operated upon four and a half years previously. Showing sebaceous gland and hair-follicle in wall, with marked leucocytic infiltration internally.

manner small atheromatous and sudoriparous cysts may be formed in the substance of the wall itself.

Peculiar inflammatory or ulcerative changes frequently take place in the walls of old orbital dermoid cysts, resulting in the formation of masses of granulation tissue. Wherever the epithelium is destroyed it is not re-formed. The hairs are thrown off and lie imbedded in granulation tissue. This invades the cavity of the cyst, but it also insinuates itself beneath the epithelium, which becomes exfoliated. In this manner the whole cyst-wall may become denuded of epithelium. The sebaceous glands are also destroyed, but the sudoriparous glands often escape this fate, owing to their position in the deeper layers of the chorion. There may be numerous mast-cells (Peschel).

The granulation tissue at first contains no vessels. It is chiefly

remarkable for the extraordinary number and size of the giant-cells found in it (Fig. 526). These are the common "foreign body giant-cells" often present in granulation-tissue, but their profuse development points to some unusual irritation. This has been found by some in the hairs, which are supposed to act as foreign bodies (Hildebrandt, Goldmann). Mitvalsky considers that the contents exert mechanical and chemical influences, which act with more severity owing to the lack of recuperative power in the abnormal epithelium.

The greater the number of giant cells, the less seems to be the tendency to organisation. Under these circumstances the cyst-wall becomes converted into a soft, pulpy mass, incapable of resisting outside pressure. The inherent tendency of granulation tissue to organise is

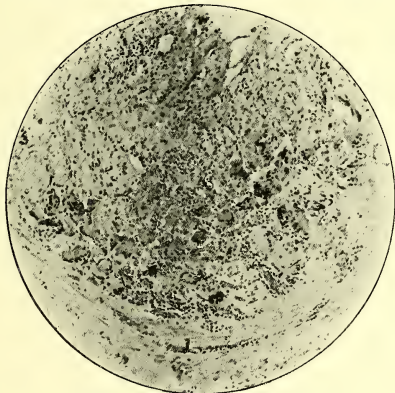


FIG. 526.—DERMOID CYST. $\times 80$.

From the same specimen. The epithelial lining of the cyst has been entirely destroyed by exuberant granulation tissue containing numbers of enormous giant-cells.

always present, and may result in the transformation of the mass into a fibrous cicatrix. The organising tissue is well supplied with vessels, which subsequently undergo degenerative changes, often accompanied by lymphocytosis. The presence of cartilage and even true bone in some of the cysts has been attributed to further pathological changes resulting from the ulcerative process (Lagrange); it is more probably a further stage in the teratoid development.

The cause of these inflammatory changes is to be sought in the continuous over-distension of the cyst (Mitvalsky). Injury seems to play no part as a rule, though when present it produces the same results. The possibility of endogenous infection must not be disregarded (Lagrange); there is, however, little evidence in its favour.

The contents of the cyst are composed of the secretions of the glands

—sebaceous material and sweat—together with cast-off hairs and corneous epithelium. Of these, the last-named usually predominates, so that the cysts assume an atheromatous character. The sebaceous constituent may predominate, resulting in an oily cyst (*cf.* Chavasse), but all combinations may occur. The oily material may be very yellow, due to oleates, or quite white, consisting of stearates and palmitates. Vassaux and Broca consider that the opaque fatty contents may be transformed into oily material subsequent to their deposition. On the other hand, an oily cyst may be transformed into an opaque one, at any rate after puncture (Chauvel), and an opaque one into an oily one after the same treatment (Lannelongue). The contents may be almost entirely epithelial, and these cysts have been described as *cholesteatomata* of the orbit. According to some authors (*e. g.* Lagrange) these tumours are of different origin. They are very rare, and are said to be sub-periosteal, whereas the true dermoid cysts are intra-periosteal. The most convincing case is that described by Schirmer; others reported by Rohmer, and Gosselin are doubtful.

Various theories have been advanced to account for dermoid cysts of the orbits: (1) Lebert's theory of plastic heterotopia; (2) the dermal inclusion theory; (3) the foetal inclusion theory, or theory of diplogenesis.

The theory of plastic heterotopia may be dismissed in few words. It was brought forward by Lebert in 1852, and states that, under the influence of perverted nutrition, the normal tissues may give rise to other tissues or even organs. There is no evidence in favour of this theory, at any rate outside the domain of malignant tumours.

The theory of dermal inclusion is that generally received. It was propounded by Verneuil in 1852, at the discussion on Lebert's theory, though it is often attributed to Remak (Lagrange). It states that the dermoid cyst arises from the inclusion of a pouch of skin, which is invaginated into the deeper tissues during foetal life. The theory best explains the facts, and is strongly supported by the site of election of the cysts—at or near the sites of foetal sutures and clefts. Other positions may be explained without undue credulity by the occurrence of quite abnormal invaginations. The bones of the skull are not yet fully developed at the time of the inclusion; hence adhesions to the periosteum and actual depressions or holes in the bones are readily explained. At the outer angle the adhesion is usually some millimetres above the edge of the orbit (Lannelongue). Depressions in the bone may be deep (*e. g.* 1.5 cm., Richet), and perforations large.

The theory of diplogenesis, or of an included foetus is unnecessary and improbable as an explanation of ordinary dermoid cysts, but it is difficult to explain the rarer teratoid tumours without having recourse to it. The presence of cartilage, bone, smooth and striped muscle, teeth, etc., in these growths cannot be explained by the dermal inclusion theory. The fullest record of an orbital teratoma is that published by Weigert in 1876. The tumour was a multilocular cyst, the size of an orange, containing epithelium—stratified, cylindrical, and ciliated—cartilage and bone, smooth muscle-fibres, and glands resembling Lieberkühn's. There is a remarkable orbital teratoma of the *fœtus in*

fœtu type in the Gynæcological Museum at Leipzig; a mass projecting from the left orbit has the characters of a left lower extremity (Ahlfeld).

LEBERT.—*Mem. de la Soc. de Biol.*, v, 1852. LAWRENCE.—*London Med. Gaz.*, 1838. MACKENZIE.—*Diseases of the Eye*. BARNES.—In Mackenzie, *loc. cit.* SPENCER WATSON.—*Lancet*, 1872. DE LAPERSONNE.—*A. d'O.*, xiii, 1893. BULL.—*Amer. Jl. of Med. Sc.*, 1879. PANAS.—*Gaz. méd. de Paris*, 1880. CORNWELL.—*A. of O.*, xi, 1882. VASSAUX AND BROCA.—*A. d'O.*, iii, 1883. STEINDORFF.—*C. f. A.*, xxiv, 1900. CHAVASSE.—*A. d'O.*, xxi, 1901. *MITVALSKY.—*A. f. A.*, xxxiii, 1891. HILDEBRANDT, GOLDMANN.—*Ziegler's Beiträge*, vii. CHAUVEL.—*Études ophtalm.*, 1896. LANNELONGUE AND MÉNARD.—*Affections congenitales*, 1891. SCHIRMER.—*B. z. A.*, xxxiv, 1898. ROHMER.—*Soc. franç. d'Opht.*, 1889. GOSSELIN.—In Demarquay, *Tumeurs de l'Orbite*, 1860. WEIGERT.—*Virchow's Arch.*, lxvii, 1876; in G-S, vi, 1880. AHLFELD.—*Die Missbildungen des Menschen*, Leipzig, 1880. PESCHEL.—*Hirschberg's Festschrift*, 1905.

Inclusion cysts.—Cysts formed by the inclusion of a portion of the meninges and brain are even rarer in the orbit than in other parts of the skull. They occasionally occur, however, usually at the inner angle, seldom at the outer. When the hernia is composed of the membranes only, enclosing cerebro-spinal fluid, the cyst is a meningocele; if part of the brain substance is also prolapsed, an encephalocele is formed; and if a cerebral ventricle is also involved, a hydro-encephalocele results. These cysts are characterised by greater or less fluctuation and greater or less reducibility under pressure. Reduction may be painful, and followed by convulsions or coma. Respiratory and circulatory pulsations are rare in orbital inclusion cysts, owing to the constriction of the pedicle.

As regards situation, Larger found thirteen at the inner angle, one at the outer angle, seventeen at the root of the nose, in forty-four cases. Those at the inner angle may resemble a distended lacrymal sac (Råab), and are not infrequently bilateral (Lyon, Wagner, Clar, Rippoll, de Britto). They are also often double in this situation; elsewhere they are usually uni-, rarely multi-ocular. They may be as large as a large hen's egg. They are seldom so pedunculated as to allow of free movement.

The invariable greater or less deformation of the skull bones is of diagnostic importance. The hernia generally passes between the ethmoid and the frontal bones, at the expense of the horizontal plate of the ethmoid; the orbital opening is at the junction of the frontal, lacrymal, and nasal process of the superior maxilla. The line of exit follows the line of the first branchial cleft (Larger). Others pass through the sphenoidal fissure or optic foramen (Talko, van Duyse). The orifice is rounded, with sharp, though smooth edges; it may be extremely small, or large enough to admit the finger.

Histologically, the outer covering is fibrous, corresponding with the dura mater. This may be adherent to thinned and very vascular skin. The arachnoid and pia mater are so altered as to be scarcely recognisable. The brain substance is œdematous and degenerated; in hydro-encephalocele it is covered on the inner side with ependyma, which is often well preserved.

Comparatively few of these cysts have been exhaustively examined histologically, so that it is difficult to say which is really the commonest. Probably most, if not all, contain some nerve substance which has

undergone cystic degeneration (v. Bergmann), and pure meningocele has been denied (Houel). Pure encephalocele has been described by Breschet, and a case of hydro-encephalocele has been very thoroughly reported by van Duyse and Moyart. The hernia may even invaginate the eyeball, as in a case reported by Krückmann, which will receive attention elsewhere.

Inclusion cysts are probably due to arrested development of the skull bones whilst they are still membranous (Meckel, Geoffrey Saint-Hilaire, Larger, Berger, and others). Various other theories need only be mentioned here: (1) arrested ossification (Corvinus (1749), Niemeyer, Klementowski); (2) premature ossification (Kuster, Ackermann); (3) cystic pachymeningitis (Spring); (4) hydrocephalus (Houel, Spring).

BRESCHET.—Arch. de Méd., xxvi, 1831. LYON.—Gaz. méd., 1843. CLAR.—Wiener Zeitschrift, vii, 1851. RIPPOLL.—In Lagrange, *Tumeurs de l'Œil*, ii, Paris, 1904. DE BRITTO, A. d'O., xxiv, 1904. RAAB.—Wiener med. Woch., 1876. LARGER.—Arch. gén. de Méd., 1877. VAN DUYSSE and MOYART.—A. d'O., xvii, 1897. BATTEN.—T. O. S., xviii, 1898. KRÜCKMANN.—A. f. O., xlvii, 1, 1899. HOUEL.—Arch. gén. de Méd., 1859. NIEMEYER.—De Hernia cerebri congenitale, Halle, 1833. KLEMENTOWSKI.—Jahr. f. Kinderheilkunde, 1862. KUSTER.—Monatsschrift f. Geburtskunde, xxxiv. ACKERMANN.—Die Schädeldeformität bei der Encephalocele congenita, Halle, 1888. SPRING.—Mém. de l'Acad. royale de Belgique, iii, 1854. BERGER.—Revue de Chirurgie, 1890. KLINGELHÖFFER.—A. f. A., xxxv, 1897. MITTENDORF.—New York Med. Rev., 1890. V. BERGMANN.—Handbuch d. prakt. Chir., i, 1899. TALKE.—In Nagel's Jahresbericht, 1900. LAGLEYZE.—A. d'O., xx, 1900. STADTFELDT.—In C. f. A., xxviii, 1904. *VAN DUYSSE.—Encyclopédie franç. d'O., ii, Paris, 1905.

ACQUIRED CYSTS

Implantation cysts of the conjunctiva have already been considered (Vol. I, p. 112). When these are deep they may be described as orbital. They are rare, and are difficult to distinguish from the rare dermoids which are devoid of hairs and glands. The best authenticated case is that of Critchett and Griffith. It followed a severe sword wound, and was discovered subsequent to the removal of the shrunken globe. It was the size of a horse-chestnut, and contained clear straw-coloured fluid. The wall consisted of dense fibrovascular tissue lined with stratified epithelium; there were no glandular structures or hair-follicles.

CRITCHETT AND GRIFFITH.—T. O. S., xvii, 1897.

Serous cysts.—The eyeball is surrounded by a serous sheath, the capsule of Tenon, which is invaginated by the extrinsic muscles. Fluid occasionally accumulates in Tenon's capsule, which assumes the nature of a cyst, pushing the globe directly forwards. The condition is in reality a so-called Tenonitis, and is rare. It may go on to the formation of pus, which is sometimes cheesy and suggestive of tubercle, as I have once seen. Only one case of Tenonitis has been examined anatomically, the eye having been removed through an error of diagnosis (Carron du Villards). There was much distension of Tenon's capsule, and the eye had no gross lesion, though it was blind, possibly due to optic neuritis.

Serous cysts in connection with the sheaths of the extrinsic muscles have been described, generally in connection with the levator palpebræ

and the superior oblique at the trochlea. If they exist, which is doubtful, they are probably of the nature of a teno-synovitis.

Serous cysts may follow hæmorrhage into the orbit, resulting from degeneration of the blood-clot. Others, possibly of the same origin, may occur in relation with orbital growths, and may even surround them (Lagrange).

CARRON DU VILLARDS.—Ann. d'Oc., xl, 1858. LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904.

PARASITIC CYSTS

Hydatid cysts of the orbit are rare (1 in 136 cases of hydatids, Cobbold); Berlin (1880) collected 39 cases, Lagrange (1904) 32 more, and there are a few which these authors have missed. They occur in any part of the orbit, slightly more commonly below, and up and out. Unlike hydatids in other parts of the body, they show no special preference for the muscles, though such have been described (Fieuzal, Brailey). It is very exceptional for them to originate in the orbital walls; a doubtful case was reported by Keate. They may invade the walls and cranial cavity, etc., secondarily (Petit, Westphal), or the orbit from the cranium (Verdalle). They usually vary in size from a pea to a nut, though they may become as large as a large orange (Keate, Westphal, de la Pena). They are at first spherical, other shapes resulting later from external pressure. They are remarkably free from adhesions to neighbouring structures, these being probably always due to injury, followed by inflammation. Growth is usually slow (six years, McGillivray; seven years, Lawrence; seven to eight years, Lawson); though it is sometimes apparently very rapid (six days, Weeks; one month, Schmidt).

Most cases of hydatid cysts in the orbit occur in young people (two thirds of the cases between 11 and 21, Neisser); only 2 out of 36 patients were over 40 (Lawford). Males are affected slightly more than females (in 46 cases 25 males, 14 females, 6 unknown, Lawford); the opposite is the case, however, taking all parts of the body (233 men to 436 women, Neisser).

Brood capsules and heads are formed later in echinococcus cysts than in most others (Leucart); they are more commonly absent than present in man, and even more so in some situations than in others, the orbit being one. When scolices or hooklets are found in the fluid they are absolutely pathognomonic.

The cyst wall has the characteristic lamination of all hydatid cysts. Thierfelder had the opportunity of examining the cyst wall in its original surroundings (v. Zehender's case). The cyst was imbedded in highly vascular tissue, which was infiltrated with inflammatory cells. The muscles had undergone colloid degeneration. There are rarely brood capsules and scolices on the inner surface of the mother cyst, but these, when they occur, are generally formed in daughter cysts, which themselves arise from the germinal layer of the mother cyst, or from brood capsules or scolices. The daughter cysts may reach 100 (Westphal), as compared with several thousands in the liver.

The fluid contents show no cells, like serous cysts, nor fat, like dermoids. It remains clear on boiling, and on the addition of acids. It is usually neutral in reaction; specific gravity, 1009 to 1015. It contains no albumen, but large quantities of sodium chloride. It often contains grape sugar, sometimes succinic acid (Heintz, Bödecker, Naunyn), and inosit (Wyss, Naunyn, Jacobson). Jacobson found 0.54-0.84 per cent. of sodium chloride; this may be tested for by silver nitrate. Small quantities of albumen may be found after the echinococcus is dead, or after rupture or puncture. The fluid is clear at first, but becomes milky after the death of the parasite. After rupture of the cyst the walls fall together, calcium carbonate and phosphate are deposited, as well as cholesterin, and suppuration often takes place. The eyeball may be destroyed by pressure or exposure due to the proptosis.

PETIT.—Œuvres complètes, 1774. SCHMIDT.—Ueber die Krankheiten des Thränenorgans, Wien, 1803. KEATE.—Med.-Chir. Trans., x, 1819. LAWRENCE.—Med.-Chir. Trans., xvii, 1820. BOWMAN.—Med. Times and Gaz., v, 1852. NAUNYN.—Arch. f. Anat. u. Phys., 1863. HULKE.—R. L. O. H. Rep., iv, 1865. MCGILLIVRAY.—Australian Med. J., 1866. VERDALLE.—Bordeaux médicale, 1872. WESTPHAL.—Berliner klin. Woch., 1873. HIGGENS.—Lancet, 1876. LAWSON.—Lancet, 1876. *NEISSER.—Die Echinokokkenkrankheit, Berlin, 1877. DE LA PENA.—La Oftalm. practica, 1881. MULES.—T. O. S., iii, 1883. DIEU.—Rec. d'O., 1884. v. ZEHENDER, K. M. f. A., xxv, 1887. BRAILEY.—T. O. S., vii, 1887. WEEKS.—A. of O., xviii, 1889. ROCKLIFFE.—T. O. S., ix, 1889. BARRETT.—Australian Med. J., 1892. MONREAL MARIN.—El Progreso medico, 1894. *LAWFORD.—T. O. S., xv, 1895. MANDOUR.—Thèse, Paris, 1895. *GOLOWIN.—Z. f. A., iv, 1900 (Bibliography). CHIRON DE BROSSAY.—Thèse, Paris, 1901. *CABAUT.—Woch. f. Ther. u. Hyg. des Auges, 1904. MARSHALL.—Ophthalmoscope, ii, 1904. COLLUCCI.—Ann. di Ott., xxxiii, 1904. *KRAEMER.—In G-S., x, 1899. *LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904.

Cysticercus cysts.—Cysticercus in the orbit is much rarer than inside the eye; only nine undoubted cases are on record. Young people and women are most affected. Two cases were near the lower orbital margin (v. Graefe, Piccoli), two near the upper margin towards the root of the nose (Horner, Badal, and Fromaget); they are seldom deep in the orbit (Higgins—a doubtful case), or within Tenon's capsule (Meyer, Sgrosso). They reach the size of a pea or bean, and frequently set up severe inflammatory symptoms. Exophthalmos (Sgrosso) is unusual, owing to the small size of the tumour, but slight dislocation of the globe leads to diplopia. Pressure and inflammatory changes may cause optic neuritis, ptosis, and paresis of the extrinsic muscles.

In v. Graefe's case the tumour was 10 mm. long, composed of dense fibrous tissue; the dead parasite lay surrounded by pus. In Horner's case the cysticercus was 1½ cm. long, with 30 hooklets on the head, arranged in two rows. In Badal's case, carefully examined by Fromaget, the fibrous hyperplasia and purulent infiltration were also noticeable; the entozoon was shrunken, but the four suckers and double row of hooklets could be made out. There are often adhesions to the periosteum or muscles.

A few cases of cysticercus in the lids and subcutaneous tissue near the orbit may be conveniently referred to here (Sichel, Canton, Hirschberg, Gros, Streatfield).

V. GRAEFE.—A. f. O., xii, 2, 1866. HORNER.—K. M. f. A., ix, 1871. HIGGENS.—Trans. Clin. Soc., x, 1877. BROWN.—Brit. Med. J., 1884. GONELLA.—Ann. di Ott., xviii, 1889. MEYER.—Rev. gén. d'Oph., 1893. SGROSSO.—Rec. d'O., xii, 1893. LECOMTE.—Thèse de Bordeaux, 1895. BADAL, FROMAGET.—A. d'O., xvi, 1896. PICCOLI.—Lav. della Oc. della R. Univ. di Napoli, v, 1897. SICHEL.—Rev. méd.-chir. de Malgaine, 1847. CANTON.—Ann. d'Oc., xxxvi, 1858. DOLBEAU.—Bull. de la Soc. d'Anat., 1861. GROS.—Gaz. des Hôp., 1871. STREATFIELD.—R. L. O. H. Rep., vi, 1872. HIRSCHBERG.—Berlin. klin. Woch., vii, 1870; xxix, 1892; C. f. A., iii, 1879. *KRAEMER.—In G-S., x, 1899.

Filaria, although not forming cysts, may be conveniently referred to here. *Filaria loa* occurs in the orbit as well as under the conjunctiva; indeed, the sub-conjunctival worms frequently retreat into the depths of the orbit, and remain quiescent there for a variable time (see Vol. I, p. 117).

ARGYLL ROBERTSON.—T. O. S., xv, 1895; xvii, 1897.

TUMOURS

Tumours of the eyeball and optic nerve have already been considered; those of the lacrymal gland will be described separately. There remain, therefore, the tumours of the walls of the orbit and of the orbital contents other than the globe, optic nerve, and lacrymal gland for consideration in this chapter.

Tumours of the orbit are best classified according to the structures from which they arise; since a great variety of structures are found in this situation the nature of these tumours is similarly diverse. They may be divided into (1) those arising from the orbital contents, (2) those arising from the walls of the orbit. To the first class belong (1) hæmangioma, (2) lymphangioma, (3) lipoma, (4) fibroma, (5) lymphoma, (6) neuroma, simple and plexiform, (7) sarcoma, including endothelioma. To the second class belong osteomata, and secondary growths originating in the frontal, ethmoidal, sphenoidal sinuses, etc.

As regards the frequency of orbital tumours, Schaaf found 46 cases in 40,415 patients at the Giessen clinic during twelve years; 12 were primary, derived from the orbital walls or contents other than the eyeball. The cases included 20 sarcomata, 13 carcinomata, 6 dermoid cysts, 2 osteomata, 1 ethmoidal mucocele, 1 echinococcus cyst, 1 lipoma, 1 glioma, 1 tumour not examined.

*LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904. SCHAAF.—Dissertation, Giessen, 1903.

HÆMANGIOMA

The first case of hæmangioma of the orbit on record was published by Abernethy (1810), but the diagnosis is doubtful. The first incontestable case is by Walton (1853). Broca (1856) described another "erectile tumour" of the orbit, being doubtful of the diagnosis because it was circumscribed; this is, however, not uncommon. In 1860 v. Graefe reviewed the subject, and defined the clinical characteristics. Berlin (1880) collected 54 cases, but several of these are demonstrably wrong diagnoses. Lagrange (1904) has collected 83 cases, including some doubtful ones. The numbers afford little evidence as to frequency, the condition being not very uncommon.

Orbital hæmangioma usually causes proptosis, which is increased by all causes which impede the venous outflow from the orbit, *e. g.* crying in children, struggling, pressure on the jugular vein (Dolgenkow), menstruation (Nelaton), etc. It may disappear after a night's rest (de Wecker), and the variations in volume may be absent in the more solid growths (van Duyse, angio-lipoma; Neese, angio-fibroma). The exophthalmos is rarely straight forwards (4 out of 15 cases, Lagrange). The compressibility of the tumour is often a marked feature, so that the proptosis may disappear after gentle continuous pressure. Simple angioma seldom, if ever, pulsates, nor is there a bruit. Pupillary and ophthalmoscopic abnormalities, defects of vision, etc., result from pressure. The disease may be associated with angiomata of the skin of the lids, etc. (Abernethy, Knapp, Martin, and others). Some cases seem to have been accompanied by encephalocele (*v.* Oettingen), hypertrophy of the thyroid (Eloui), and malignant development in the tumour has been cited (Sokoloff, Panas). Panas found an abscess in an angioma containing typhoid bacilli, during the course of typhoid fever.

Virchow divided angiomata into simple (telangiectasis) and cavernous. Simple hæmangiomata consist of a network of dilated capillaries; van Duyse's angio-lipoma belongs to this class, which is uncommon in the orbit (Ricci, Manz, Gosetti). Telangiectases usually have no capsule.

Cavernous angiomata are much commoner in the orbit. They are generally rounded tumours, with a knobby surface, quite circumscribed, and usually encapsuled. They vary in size; the largest, an angio-fibroma, was 6 cm. in diameter (Neese). These tumours sometimes contain calcareous concretions or phleboliths (Samelsohn, van Duyse).

The capsule, which is generally present, consists of fibrous tissues arranged in more or less concentric laminæ, containing some elastic fibres. Processes are sent inwards to form a coarse network of trabeculæ, which separate the blood-spaces. These are lined with endothelium, so that the structure exactly corresponds with that of normal erectile tissue, *e. g.* penis, etc. (Fig. 61, Vol. I). The trabeculæ often contain deposits of pigment, which is hæmatogenous in origin (Campart); the endothelium may also contain pigment (Panas). The growth sometimes contains unstriated muscle (Coppez).

The alveoli contain pure blood, though some may be emptied by manipulation. Cornil and Ranvier noted the infrequency of white corpuscles. The red corpuscles are generally closely packed together. Some of the alveoli may be much enlarged, so that the tumour has the character of a cyst; whether this occurs as a degenerative phenomenon (Valude) is doubtful. It has been described as a sequel to electrolysis (Lagrange). The growths may certainly undergo fibrous degeneration (de Wecker, Neese), and this probably accounts for the angio-fibromata. Angio-lipomata also occur (van Duyse, Ahrens). The cases described as becoming malignant are doubtful, though analogy would lead one to anticipate the possibility of such an occurrence. Spontaneous disappearance has not been observed in orbital hæmangiomata.

Hæmangiomata usually occur in young people—29 cases under

20 years, 21 between 20 and 40, 10 over 40 (Fermond); oldest *æt.* 60 (Gosetti); they are often, possibly always, congenital. They are ascribed by Virchow to slight irritation, affecting highly vascular free edges and surfaces. Usually there is extensive new formation of capillaries, resulting in slowing of the blood-flow; gradual dilatation follows, causing free communication between arteries and veins, so that a condition approximating that of arterio-venous aneurism is set up, and still further dilatation accrues. Some of the walls give way, and thus cavernous spaces are formed. Rarely the arterioles suffer most, and the growth resembles a cirroid aneurism; but usually the vessels are most affected towards the venous side.

ABERNETHY.—Surgical Observations, 1810. WALTON.—Operative Ophthalmic Surgery, 1853. V. GRAEFE, A. f. O., vii, 2, 1860; xii, 2, 1866. HODGES.—Boston Med. and Surg. J., 1864. RICCI.—Dublin Quarterly J., 1865. JEAFFRESON.—R. L. O. H. Rep. vii, 1871. LAWSON.—Lancet, 1871; 1875. SPENCER WATSON.—Brit. Med. J., 1873. GOSETTI.—Ann. di Ott., vii, 1878. SAMELSON.—In G.-S., vi, 1880. ELIOT.—A. d'O., ii, 1882. PANAS.—A. d'O., iii, 1883. CAMPART.—Bull. des Quinz-Vingts, 1884. VAN DUYSSE.—In Lagrange. EMRYS-JONES.—T. O. S., ix, 1889. AHRENS.—K. M. f. A., xxvii, 1889. KNAPP.—A. of O., xxv, 1890. *NEESE.—A. f. A., xxxv, 1897 (Bibliography). USHER.—Brit. Med. J., 1898. SOKOLOFF.—Z. F. A., i, 1898. BULL.—T. Am. O. S., 1900. WHITEHEAD.—Brit. Med. J., 1901. PARINAUD AND ROCHE.—Ann. d'Oc., cxxvi, 1901. HOLMES SPICER.—T. O. S., xxiii, 1903. *LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904 (Bibliography).

LYMPHANGIOMA

There are only five cases of lymphangioma of the orbit on record (Förster, Wiesner, Silcock, Ayres, Wintersteiner). The tumours are small and increase in size very slowly. They are probably congenital, though the ages of the patients were 46, 43, 21, 53, and 12 respectively. The structure is that of cavernous hæmangiomas, except that the spaces contain lymph instead of blood. Some of the spaces contained blood in Wintersteiner's case, and diagnosis rested on continuity with the perivascular lymphatics of the long posterior ciliary arteries. It is obvious that confusion may easily arise from this cause (*v.* Vol. I, p. 126). The tumours observed have been inside the cone of extrinsic muscles.

FÖRSTER.—A. f. O., xxiv, 2, 1878. WIESNER.—Dissertation, Würzburg, 1886. AYRES.—Amer. J. of Ophth., 1895. SILCOCK.—T. O. S., xvi, 1896. *WINTERSTEINER.—A. f. O., xlv, 3, 1898.

LIPOMA

Apart from congenital fibro-fatty tumours (Vol. I, p. 135) the cases which have been described as lipomata of the orbit are all open to doubt. The large amount of normal fat in this situation accounts for much of the difficulty. In Puccioni's case the tumour was said to be encapsuled. Dupuytren's case was probably a dermoid cyst; Cornaz, a dermo-lipoma; those of Carron du Villards, Travers, and others, simply normal orbital fat. A case by Gross is insufficiently reported. Knapp described three lipomata in an orbit, two above and one below.

Angio-lipomata have been reported several times, but here the hyperplasia of adipose tissue is secondary and adventitious. Knapp's

case was essentially an angioma with fibrous hyperplasia; van Duyse's has already been referred to (p. 727).

Lipomata, involving the lids, have been mentioned in Vol. I (p. 18). Most of these are rather due to hernia of orbital fat than to true new formations (Schmidt-Rimpler). They may be congenital and bilateral (Bowman, Armaignac).

DUPUYTREN.—*Lancette française*, 1835. CORNAZ.—*Des Abnormalités congénitales des Yeux*, 1848. CARRON DU VILLARDS.—*Ann. d'Oc.*, xl, 1858. TRAVERS.—*Synopsis of Diseases of the Eye*. KNAPP.—*Comptes rendus du Congrès internat.*, Utrecht, 1899; *A. f. A.*, vi, 1877. SCHMIDT-RIMPLER.—*C. f. A.*, xxiii, 1899. BOWMAN.—*London Jl. of Med.*, 1849. ARMAIGNAC.—*Rev. clin. d'Oc.*, 1886. GRUENING.—*T. Am. O. S.*, 1898. PUCCIONI.—*Ann. di Ott.*, xxxii, 1903.

FIBROMA

The occurrence of simple fibroma in the orbit has been denied, and it must be admitted that other neoplasms, notably endotheliomata, may easily be mistaken for them. Lagrange has collected cases more or less probable by Hope, Verhaege, Mackenzie, Critchett, Secondi, Schiess-Gemuseus (?), Horner, Perls, Despagne, Badal (2), Fano, Piechaud and Ussel, Tornatola (?), Goldzieher.

Fibromata probably arise almost invariably from the periosteum or the dural sheath of the optic nerve; they are therefore considered here only for convenience. It is possible that they may spring from the tendons (Gonin). The best test of a simple fibroma would seem to be encapsulation, the fibrous tissue composing the growth being matted together at the periphery. Fibromata may be hard or soft, the latter being due to œdema or possibly myxomatous degeneration (Tornatola); there are no chemical tests recorded which prove the presence of mucin. Softening may go on to the formation of cystic spaces (Schiess-Gemuseus, Horner), though such tumours are open to other interpretation. Patches of adipose tissue were found in Perl's tumour, which filled the orbit, the roof being perforated; such patches indicate infiltration of the orbital fat (*cf.* p. 706), and are suggestive of malignant hyperplasia rather than of a simple fibroma. Endotheliomata require careful examination in some cases to distinguish them from simple fibromata (*v. infra*), and it is not unlikely that further research will eliminate simple fibromata from the list of orbital growths.

Fibrous changes in angiomata have been referred to (p. 726); Gonin's subconjunctival tumour arising from the external rectus was such an angio-fibroma.

HOPE.—*Phil. Trans.*, xliii, 1744. VERHAEGE.—In Demarquay, *Tumeurs de l'Orbite*, Paris, 1860. MACKENZIE.—*Diseases of the Eye*. CRITCHETT.—*Med. Times and Gaz.*, 1852. SECONDI.—*Giornale di Ott.*, 1866. SCHIESS-GEMUSEUS.—*A. f. O.*, xiv, 1, 1868. HORNER.—*K. M. f. A.*, ix, 1871. PERLS.—*Berliner klin. Woch.*, 1874. BADAL.—*Leçons d'Opht.*, 1879; *A. d'O.*, xi, 1891. TORNATOLA.—*Ann. di Ott.*, xviii, 1889. GOLDZIEHER.—*C. f. A.*, xviii, 1894. GONIN.—*A. f. A.*, xxxix, 1899. REID.—*T. O. S.*, ix, 1889.

LYMPHOMA

As has already been pointed out (Vol. I, p. 18) the tumours classified as lymphomata are of uncertain pathological significance, including

growths variously described as lymphadenomata (Hodgkin, 1832), lympho-sarcomata, leukæmic tumours, chloromata, etc. In the present state of uncertainty Hochheim's classification into (1) simple lymphoma, (2) leukæmic tumours, (3) pseudo-leukæmic tumours, and (4) doubtful cases may be adopted. Many cases must be included in the fourth group owing to insufficient details, especially as to the condition of the blood.

The reported cases may be provisionally grouped thus:

(1) *Lymphoma*.—Becker-Arnold, Bernheimer, R. Schirmer, Silcock, Gayet (Case 1), Westhof.

(2) *Leukæmic tumours*.—Gallasch, Chauvel, Leber, Osterwald, Birk, Delens, Dunn, Kerschbaumer, Valude and Morax. *Chloroma*.—Rosenblath, Cirincione, Ayres, Chiari, Körner, Behring and Wicherkiewicz.

(3) *Pseudo-leukæmic tumours*.—Tomasi-Crudeli, Corrado, Oxley, Reymond, Guaita, Axenfeld, Treacher Collins, Fröhlich, Boerma, Panas, Bronner, Ahlström.

(4) *Doubtful cases*.—Powell, de Wecker, Gayet (Case 2), Birch-Hirschfeld.

These tumours are generally symmetrical, affecting both orbits and often all four lids; sometimes the walls of the globe are infiltrated (Coppez), and even the uveal tract (Gayet). All present similar anatomical features—very densely packed cells, in every respect resembling lymphoid cells, with an extremely fine reticulum, so fine, indeed, that it is often demonstrable only with difficulty. In many cases there is definite leukæmia, and in others there can be little doubt that the blood is profoundly altered.

The term "chloroma" indicates the yellowish-green coloration of some of the growths, due to a hæmatogenous, or possibly fatty (Huber, Chiari) pigment. This is probably adventitious, and of no special significance. Such chloromata, however, generally affect the orbit (16 out of 22 cases), sometimes invading it secondarily from the antrum of Highmore (Chiari), the cranial cavity (Huber), the ethmoidal and sphenoidal cells (Behring and Wicherkiewicz), etc. They are also sometimes bilateral (Körner, Ayres, Chiari). Some authors consider that they are sarcomata (Huber, Risel, Chiari, Körner), probably originating in the periosteum; others regard them as lymphomata (Waldstein, v. Recklinghausen, Axenfeld), arising from the lymphatics. They are generally multiple.

Lymphomata do not contain true giant cells, nor do they caseate. They often show hæmorrhages in various stages of absorption. They occur at all ages from $4\frac{1}{2}$ years (Gallasch) to 70 (Gayet, Panas).

It is often impossible to determine the exact site of origin, and hence whether the growths are really multiple or invade the other orbit by continuity. The undoubted sarcomata are seldom, though occasionally (Birch-Hirschfeld) bilateral, and this is *prima facie* evidence against malignancy. Microscopically, in the present state of knowledge, it is often impossible to be certain on this point. The independence of the two growths is undoubted in some cases (Treacher Collins, Colucci, de Schweinitz, Mooren, Körner): transference by way of the optic nerves and chiasma is the greatest rarity. On the other hand, Birch-

Hirschfeld has demonstrated continuity by way of the nasal or sphenoidal cavities in one case. The tumour was extremely malignant and contained a mass of cartilage in the same position in each orbit, a fact which points to a congenital origin.

As regards the ontogeny of orbital tumours Kundrat goes so far as to say that they are all congenital, arising from foetal rests. The time of their proliferation depends upon some intercurrent circumstance, and may be deferred until late in life.

Amongst the doubtful tumours Wingenroth's case may again be mentioned (Vol. I, p. 18).

HODGKIN.—*Med.-Chir. Trans.*, xviii, 1832. Discussion on Lymphadenoma, *Trans. Path. Soc.*, liii, 1902. BECKER and ARNOLD.—*A. f. O.*, xviii, 2, 1872. BERNHEIMER.—*K. M. f. A.*, xxvii, 1889. SCHIRMER.—*K. M. f. A.*, v, 1867. SILCOCK.—*T. O. S.*, viii, 1888. GAYET.—*A. d'O.*, vi, 1886. WESTHOF.—In Panas, *Traité*, ii. GALLASCH.—*Jahrb. f. Kinderhik.*, 1875. CHAUVEL.—*Gaz. hebdomadaire*, 1877. LEBER.—*A. f. O.*, xxiv, 1, 1878. OSTERWALD.—*A. f. O.*, xxvii, 3, 1881. BIRK.—*St. Petersburg. med. Woch.*, 1883. DELENS.—*A. d'O.*, vi, 1886. DUNN.—*Ophth. Rev.*, xiii, 1894. KERSCHBAUMER.—*A. f. O.*, xli, 3, 1895. VALUDE and MORAX.—In Lagrange, *Tumeurs de l'Œil*, ii, 1904. ROSENBLATH.—*Deutsches Arch. f. klin. Med.*, lxxii. AYRES.—*Jl. Amer. Med. Assoc.*, xi, 1896. CHIARI.—*Prager Zeitschr. f. Heilk.*, iv, 1882. KÖRNER.—*Zeitschr. f. Ohrenhik.*, xxix, 1896. BEHRING and WICKERKIEWICZ.—*Berliner klin. Woch.*, xxxiii. HUBER.—*Arch. f. Heilk.*, xix. CIRINCIONE and CALDERARO.—*La Clinica oculistica*, 1903. TOMASI-CRUDELI.—*Virchow-Hirsch Jahresbericht*, 1871. OXLEY.—*Brit. Med. Jl.*, 1872. REYMOND.—*Ann. di Ott.*, xii, 1883. GUAITA.—*C. f. A.*, xiv, 1890. AXENFELD.—*A. f. O.*, xxxvii, 4, 1891. JULER.—*T. O. S.*, xii, 1892. TREACHER COLLINS.—*R. L. O. H. Rep.*, xiii, 1893. FRÖHLICH.—*Wiener med. Woch.*, 1893. BOERMA.—*A. f. O.*, xl, 4, 1894. PANAS.—*Traité*, ii. BRONNER.—*Trans. of the Internat. Congress, Edinburgh*, 1894. AHLSTRÖM.—*K. M. f. A.*, xlii, 1904. POWELL.—*Tr. Path. Soc.*, xxi. DE WECKER.—In de Wecker and Landolt, *Traité*, iv, 1889. *HOCHHEIM.—*A. f. O.*, li, 2, 1900. *BIRCH-HIRSCHFELD.—*A. f. O.*, lvi, 3, 1903. GOLDZIEHER.—*Z. f. A.*, vii, 1902. ROLLET.—*Rev. gén. d'O.*, 1903.

NEUROMA

Simple neuroma has seldom been described in the orbit, probably owing to the small size and the absence of symptoms. In multiple neuromata the ophthalmic division of the fifth is often involved. Houel found several neuromata in both orbits during an autopsy. The third, fourth, and nasal and frontal branches of the fifth nerves were affected. Bietti has described amputation neuromata of the ciliary nerves after optico-ciliary neurotomy. An isolated false neuroma or neuro-fibroma, probably of the lacrymal branch of the fifth, has been reported by Tertsch.

WHERRY.—*T. O. S.*, xii, 1892. HOUEL.—In Lagrange, *Tumeurs de l'Œil*, ii, Paris, 1904. BIETTI.—*A. f. O.*, xlix, 1900. *TERTSCH.—*A. f. O.*, lv, i, 1902. MARCHETTI.—*Ann. di Ott.*, xxxiii, 1904.

Plexiform neuroma (Verneuil), cirroid neuroma (Bruns), or elephantiasis neuromatodes of the lids is very rare; in the orbit it is still rarer (Billroth, Bruns, Marchand, Sachsaler, Rockliffe and Parsons).

Billroth in 1863 described such a tumour of the right upper lid spreading to the temporal region in a boy, *æt.* 6; in 1869 he described another, in a young man, *æt.* 18, which was congenital, as large as the fist, and involving the left upper lid and temple.

Bruns reported three cases, one in a man, *æt.* 28, and the others in

two brothers, in both of whom there was general neuromatosis, with multiple neuromata of the vagi in one.

Gengersich in 1870 reported the case of two brothers. In one there were multiple neuromata of the 3rd, 4th, 5th, 7th, 9th, 11th, and 12th nerves; in the other a swelling occurred, after an injury, in the right side of the forehead, involving the eyebrow.

Marchand, in 1877, described a plexiform neuroma of the left upper lid and temple, noticed at the age of 6 months; there was ptosis.

v. Recklinghausen, in 1882, published a book on 'Multiple Fibromata of the Skin, and their Relationship to Multiple Neuromata.' In one case there were multiple neuromata of the frontal and supra-orbital nerves, the 1st, 2nd, 3rd, and 4th cranial nerves being free. In another there was a small nodule at the edge of the left eyelid.

Herczel, in 1890, related the following case:

A boy, *æt.* 9, had a mother's mark on the left arm, which spread over the whole flexor surface, and had an increasing swelling at the upper part; there was a similar one over the left clavicular fossa. The left pupil was wider than the right and the left upper lid swollen; slight ptosis. There was a varicose swelling over the supra-orbital margin of the same side.

de Schweinitz, in 1891, reported a neuro-fibroma of the right upper eyelid and adjacent temporal region in a man, *æt.* 20. There was ptosis and thickening of the upper lid. The swelling was noticed at birth, and gradually increased, with development of slight pigmentation of the skin. In the eyelid the epithelium was thickened, the sebaceous glands were hypertrophied, and there was wide dilatation of the lymph-spaces. The growth consisted of "concentric whorls of loose, fibrous connective tissue, containing many nuclei, and in their centre medullated nerve-fibres, sometimes intact, and sometimes partially destroyed by fatty degeneration."

Jacqueau, in 1896, described a gradually increasing plexiform neuroma of the right upper lid and temporal region, causing ptosis and interference with vision.

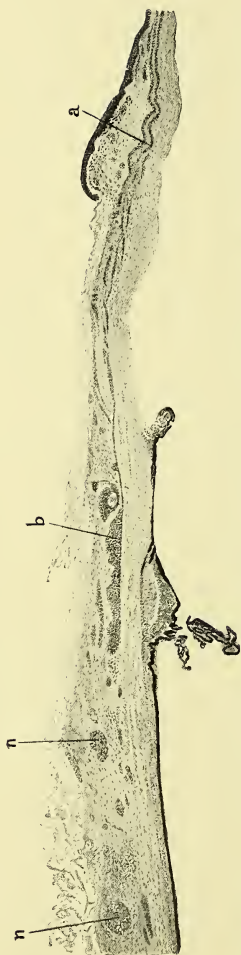
Sachs alber, in 1897, gave a very exhaustive account of a case of plexiform neuroma of the orbit, with secondary buphthalmia, in a child, *æt.* 7, the growth dating from birth. The whole of the left side of the face was enlarged, the bones being also involved. Defects in the outer wall of the orbit could be felt. The skin over the tumour showed the thickening of elephantiasis. The growth was made up of coils of enlarged and varicose nerves, lying in a mass of fibrous tissue.

Bruns also recorded a case involving the orbit.

Katz, in 1898, carefully described a plexiform neuroma of the right upper lid and orbit in a girl, *æt.* 12, who was apparently healthy until 3 years old, when she fell down twelve stairs, injuring the right side of her head. A swelling appeared in the right lid and gradually grew.

Emanuel, in 1901, discusses the relationship between optic-nerve tumours and elephantiasis neuromatodes, and their resemblance to the fibromatosis of elephantiasis has been previously insisted on by Byers.

Snéguirew, in 1900, reports a neuro-fibroma of the skin of the eyelid and head in a woman, *æt.* 24. It was situated, as usual, on the side of



the forehead (L.), and involved the upper lid and cheek, extending back to the ear. The microscopical appearances with hæmatoxylin and eosin, and with Pal, were typical. There was no basement membrane to the ducts of the sweat-glands; the other glands were normal. Many nerve-fibres without sheaths were free in the connective tissue, which confirms an observation of v. Recklinghausen's. The latter's views are also confirmed by Kriege and Unna.

Snell and Treacher Collins (1903) report three cases; in one the ciliary nerves were affected in their passage through the sclerotic, and there was buphthalmia on this side (Fig. 527). Verhoeff refers to another case with buphthalmia, and Treacher Collins and Rayner Batten (1905) to yet another.

The following is the description of a case of Rockliffe's which I examined:

Macroscopic examination. — Cornea ulcerated near the centre, bulging slightly, iris adherent. Anterior chamber absent above, where iris is adherent to cornea; shallow and slit-like below. Iris adherent to cornea above from periphery to near pupillary margin; pupil free, constricted. Lens shrunken, *in situ*. Retina oedematous, *in situ*. Choroid *in situ*. Optic disc swollen.

The growth is 25 mm. thick, measured in a direction up and back. It consists of dense fibrous tissue, which is looser near the globe, in the situation of Tenon's capsule. Running through it are several large convoluted nerve-cords, varying in size, the largest being larger than the optic nerve itself (Fig. 531).

Microscopic examination. — Cornea: epithelium irregular, shows development

FIG. 527.—PLEXIFORM NEUROMA.

Snell and Treacher Collins, T. O. S., xxiii. Ciliary region and sclero-corneal margin of a buphthalmic eye. The root of the ill-developed iris is seen to be very thin and adherent to the cornea. *a*. Thickened nerves in the cornea. *b*. Thickened perineurium around the anterior ciliary nerves in the sclerotic, cut longitudinally. *n*. Nerves in the sclerotic with thickened perineurium cut transversely.

of true papillæ over whole area and general tendency to epidermal type, but no corneous layer has yet been formed; Bowman's membrane destroyed throughout; anterior layers of substantia propria densely infiltrated with round cells; vascularised; posterior laminæ intact, œdematous, and slightly infiltrated; Descemet's membrane and endothelium intact, except where iris is adherent. The perforation is filled with a mass of granulation tissue, containing uveal pigment, and covered by ill-developed epithelium. Anterior chamber: both angles blocked by adhesion of iris to cornea at the periphery. Iris infiltrated and degenerated, especially where adherent to cornea; it is wholly

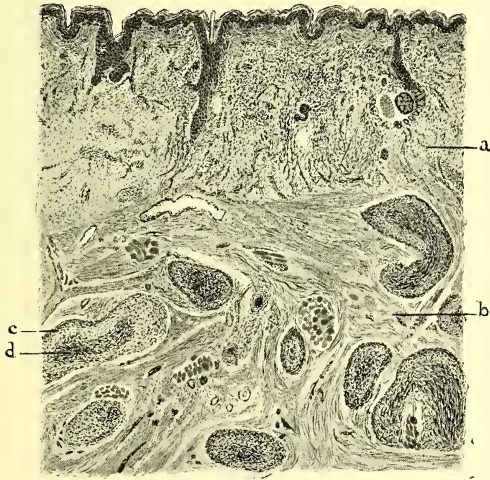


FIG. 528.—PLEXIFORM NEUROMA.

Snell and Treacher Collins, T. O. S., xxiii. Section of skin and new growth.
a. Thickened corium. *b.* Subcutaneous tissue with thickened nerves. *c.* Thickened perineurium. *d.* Nerve-fibres.

disorganised in the situation of the corneal perforation. Ciliary body atrophic. Retina degenerated; the layers are readily recognisable, including the rods and cones, but there is some infiltration of the nerve-fibre layer, especially around the vessels, and some degeneration of ganglion cells. Choroid congested and moderately infiltrated. Optic disc swollen and much infiltrated upon the surface. Optic nerve shows some infiltration along the trabeculæ, but little degeneration; the inter-vaginal space is dilated, the arachnoid being infiltrated and swollen, showing also proliferation of the endothelium.

The growth consists of coiled and convoluted nerves of the most

various sizes, surrounded by dense fibrous tissue, which infiltrates the orbital tissues, fading off imperceptibly into the orbital fat, etc. Portions of the tumour were mordanted in chrome-alum solution, stained with

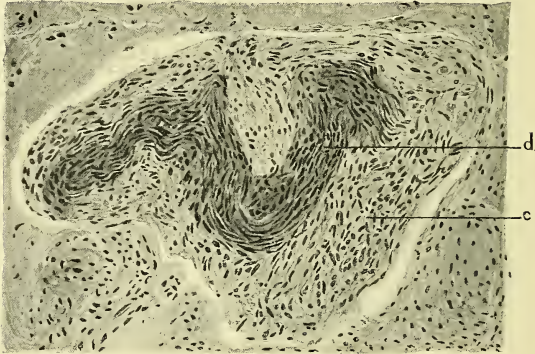


FIG. 529.—PLEXIFORM NEUROMA.

From the same specimen. One of the subcutaneous nerves more highly magnified. *c.* Thickened perineurium. *d.* Nerve-fibres with thickened endoneurium.

Kultschitzky's acid hæmatoxylin, and differentiated in the same author's solution of potassium ferricyanide in lithium carbonate. It was then seen that the nerve-cords consisted almost entirely of enormously

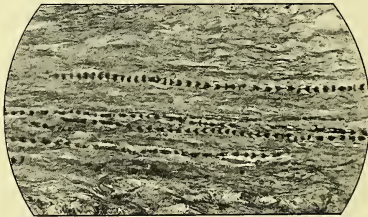


FIG. 530.—PLEXIFORM NEUROMA.

Verhoeff, R. L. O. H. Rep., xv. Plexiform neuroma of eyelid, showing arrow-head markings (Schmidt-Lantermann segments) in medullated fibres. Stained by Mallory's phosphotungstic acid hæmatoxylin.

hypertrophied sheaths, the nerve-fibres being intact, or, as seemed undoubted in some cases, degenerated. The proliferation affects the endo- and perineurium most, the epineurium least. The ciliary nerves

are affected before their entry into the eye, but not afterwards in this case.

A few curious bulbs were found, resembling end-organs (Fig. 532). They were situated, not near the surface, but deep in the tissues; they were found in only a few sections, and could not be discovered in the sections stained by the Weigert method. They consisted of a thin laminated capsule, with numerous nuclei between the layers. The body within this, stained with eosin, appeared to be convoluted, as shown by fine wavy lines, was separated slightly from the capsule (? an artefact), possessed a few nuclei limited to the periphery, and in one or two places dark bodies like nuclei more deeply situated. The latter recall the bodies described by Shattock in the terminals of *nervi nervorum*. I am not prepared to say definitely what these curious bulbs are. There can be little doubt that they are nerve-endings. They are not superficial conjunctival ones; hence they must be either nerve-endings of

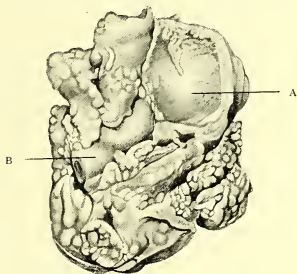


FIG. 531.—PLEXIFORM NEUROMA.

Rockliffe and Parsons, *Trans. Path. Soc.*, lv. Showing the contents of the orbit removed by operation. A. The globe of the eye. B. The enlarged optic nerve. The rest of the mass consists of nerves thickened and tortuous from fibromatosis.

nervi nervorum or of tendons, since they do not at all resemble those of muscle. As regards the first, they are neither situated in the epineurium (*cf.* Horsley)¹ nor within the perineurium (Shattock).² True end-bulbs have been observed in tendons, but are not the most common form of termination. It is unfortunate that they were absent from the Weigert sections examined. A few bodies rather like them were found in the thickened nerve-sheaths, but they were far less definite. It is interesting to remember that somewhat similar bodies led Shattock specially to examine multiple neuro-fibromata and molluscum fibrosum for them. These bodies have since been found in the choroid (*v. p.* 492).

The upper lid was enormously swollen, the increase in tissue being principally upon the posterior or conjunctival side, resulting in marked ectropion. This increase of growth consisted of the same masses of convoluted nerves, covered by inflamed conjunctiva; the nerves were

¹ HORSLEY, *Proc. of the Roy. Med. and Chir. Soc.*, 1884.

² SHATTOCK, *Trans. Path. Soc.*, xlv, p. 151.

generally smaller than the orbital ones. The other tissues of the lid exhibited mere œdema and congestion, great dilatation of the subdermal lymphatics being a marked feature (Fig. 3, Vol. I).

The whole subject has been discussed in a monograph on "Neuroma and Neuro-fibromatosis," by Alexis Thomson (1900). Many other cases (sixty-two in all) of plexiform neuroma are recorded there, affecting many parts of the body, but implication of the orbit is conspicuous by its absence. The author points out the intimate relationship between the following conditions:

- (1) Multiple neuro-fibromata (generalised neuro-fibromatosis).
- (2) Plexiform neuro-fibroma (plexiform neuro-fibromatosis).
- (3) Molluscum fibrosum (cutaneous neuro-fibromatosis).



FIG. 532.—PLEXIFORM NEUROMA. $\times 120$.

Rockliffe and Parsons, Trans. Path. Soc., lv. Showing the structures suggestive of end-organs.

- (4) Elephantiasis neuromatosa.
- (5) Pigmentation of the skin associated with neuro-fibromatosis.
- (6) "Secondary malignant neuroma" (Garré), being the sarcomatous transformation of one or other form of neuro-fibromatosis.

It may be noted that in twenty-six of the recorded cases of molluscum fibrosum the lesion was combined with tumours of the nerve-trunks in twenty-two, with pigmentation of the skin in sixteen, with plexiform neuro-fibroma in six, and with elephantiasis neuromatosa in two cases. Molluscum fibrosum may also be associated with pigmented and other moles of the skin.

In regard to the general histology and distribution of plexiform neuro-fibroma, the plexiform arrangement of the nerves can be made out by simple dissection. Long continuous nerve-cords with monili-

form enlargements of various sizes and shapes can thus be easily isolated from the surrounding loose, œdematous connective tissue.

Sections of such tumours, stained by hæmatoxylin and eosin, demonstrate the general relationships of the nerves; but special staining methods, particularly Weigert's medullary sheath-stain and its modifications (Pal, Kultschitzky, etc.), are necessary to demonstrate the condition of the nerve-fibres and sheaths. In specimens hardened in Müller's and other chrome solutions this is easy, but most specimens are now hardened first in formol. With these the only essential is that they shall not first be treated with alcohol. Formol-hardened tissues should be laid for a few days in one of the bichromate-chrome-alum solutions (*e.g.* Ford Robertson's); celloidin sections will then show the Weigert reaction well. I have myself found Kultschitzky's method quite satisfactory. Ehrlich's and the Biondi-Heidenhain triple staining solutions, as well as Finotti's method, give good results (Sachsaler).

The histological characters of plexiform neuromata were thoroughly investigated by Ziegler and Baumgarten in Bruns' specimens, and their observations have been confirmed by Goldmann, but various explanations have been adduced. *v.* Recklinghausen regards the origin of the fibromatosis as the sheaths of the vessels, and especially of the nerves; Kriege and others the sheaths of the cutaneous nerves; Lahmann and others the sheaths of the sweat-glands and hair-follicles; Jordan and Finotti the sheaths of the vessels. Finotti says that "the primary disease is in the nerves, and that this affection of the nerves causes trophic disturbances, as the result of which proliferation of the connective tissue of the sheaths of the vessels and fibromatosis of the skin and subcutaneous tissues ensue."

The nerve-fibres themselves are often intact, although displaced and dissociated; on the other hand, they are also said sometimes to degenerate, and even disappear (Baumgarten). In the specimen which I have examined there certainly appears to be some degeneration. Goldmann and Alexis Thomson regard this as altogether exceptional. The most important change found is the proliferation of connective tissue within the primary bundles of nerve-fibres; but whilst some bundles escape altogether, others are much affected. Central and peripheral bundles are affected indiscriminately. Longitudinal sections show areas of normal nerve running into bands of wavy dissociated fibres, the degree and distribution of hyperplasia and dissociation determining the amount of deviation and curvature of the nerve. Nearly all authors agree that the endoneurium is most affected, the perineurium much less or not at all, whilst the epineurium is more compact, and is free from normal fat-cells. The tissue is œdematous, with numerous lymphocytes and other cells, some about twice the size of a red corpuscle, with a small round nucleus and finely granular protoplasm; these may be proliferated endothelial cells (Finotti). The tissue is well supplied with blood-vessels.

Some authors consider that motor nerves only are affected (Sachsaler), others that only sensory nerves are involved; both views are certainly erroneous. Out of forty-five cases, for example, of generalised

neuro-fibromatosis examined by Alexis Thomson, cranial nerves were affected in about two thirds, and none of these were exempt, the vagus (twenty-nine) and trigeminal (twelve) being most commonly involved.

"The spinal and peripheral nerves would appear to be invariably affected" (Alexis Thomson). On account of the special character of the olfactory and optic nerves, as being outgrowths of the brain, true neuroma in these cases demands more thorough investigation, and may well be doubted. The sympathetic system seems specially subject to the disease.

Plexiform neuro-fibromatosis, in fifty-six collected cases, affected the temple, forehead, and upper eyelid in eighteen cases, and the posterior part of the neck and behind the auricle in fourteen cases (Alexis Thomson). It was associated with multiple neuromata in twelve of Bruns' cases, and in thirteen out of twenty collected by Alexis Thomson. It was associated with molluscum fibrosum in about the same proportion of cases.

VERNEUIL.—Arch. gén. de Méd., xviii, 1886. BRUNS.—Virchow's Arch., l, 1870. BILLROTH.—Arch. f. klin. Chirurgie, iv, 1863; xi, 1869. GENERSICH.—Virchow's Arch., xlix, 1870. MARCHAND.—Virchow's Arch., lxx, 1877. v. RECKLINGHAUSEN.—U. die mult. Fibrome der Haut u. ihre Beziehung z. d. mult. Neuromen, Berlin, 1882. HERCZEL.—Ziegler's Beiträge, viii, 1890. DE SCHWEINITZ.—Tr. Amer. O. S., xxvii, 1891. JACQUEAU.—Gaz. hebdom., 1896. SACHSALBER.—B. Z. A., xxvii, 1897. BRUNS.—Bruns' Beiträge z. klin. Chir., viii. KATZ.—A. f. O., xlv, 1898. EMANUEL.—A. f. O., liii, i, 1901. PARSONS.—T. O. S., xxiii, 1903. SNÉGUIREW.—A. d'O., xx, 1900. KRIEGE.—Virchow's Arch., cviii, 1887. UNNA.—In Orth's Pathologie, Berlin, 1894. ALEXIS THOMSON.—Neuroma and Neuro-fibromatosis, Edinburgh, 1900. GARRÉ.—Bruns' Beiträge z. klin. Chir., ix. GOLDMANN.—Bruns' Beiträge z. klin. Chir., x. LAHMANN.—Virchow's Arch., ci. JORDAN.—Ziegler's Beiträge, xviii. FINOTTI.—Virchow's Arch., cxliii. *SNELL AND TREACHER COLLINS.—T. O. S., xxiii, 1903. VERHOEFF.—In Snell and Treacher Collins. CESTAN.—Rev. neurol., 1903. *PARSONS AND ROCKLIFFE.—Trans. Path. Soc., lv, 1904. FRUGIELE.—Ann. di Ott., xxxiii, 1904. FRAENKEL AND HUNT.—Pub. of Cornell Univ. Med. Coll., i, 1904. *TREACHER COLLINS AND RAYNER BATTEN.—T. O. S., xxv, 1905.

SARCOMA AND ENDOTHELIOMA

Sarcomata of the orbit may be primary or secondary; members of each group may be non-pigmented or melanotic. As has been seen in dealing with sarcomata of the choroid, the question of pigmentation is of subsidiary importance. The further classification of sarcomata is at present in a chaotic condition; it would therefore be unwise to introduce a new classification, founded upon unproved theories; hence the old descriptive grouping will be retained, modern views being discussed incidentally.

PRIMARY SARCOMATA

Classification.—Primary sarcomata of the orbit may be classified into leuco-sarcomata and melanotic; the latter form a small group which may be considered *en bloc*. Leuco-sarcomata are conveniently described according to (1) Cytology: fibro-sarcomata, spindle-celled, round celled, etc.; (2) Angio-sarcomata: hæmangio-sarcomata and lymphangio-sarcomata, including alveolar sarcomata, cylindromata,

etc.; (3) Combined tumours: myxo-sarcomata, chondro-sarcomata, myo-sarcomata (glio-sarcomata), etc. Most of group (2), and some of groups (1) and (2) are probably endotheliomata.

Frequency.—No accurate statistics are available as to the frequency of orbital sarcomata. A general impression would lead one to suppose that they are rare, probably nearer Hartridge's estimate (1 in 10,000) than Lagrange's (1 in 1500). Stirling collected twenty-nine cases; of these twenty-seven represented all the cases examined pathologically at Moorfields from 1858 to 1893; Silcock and Marshall reported eight Moorfields cases seen between 1893 and 1899. The diagnosis is open to doubt in several of these cases. As regards *pigmentation*, primary melanotic growths are very rare; about a dozen more or less doubtful cases have been recorded.

As regards *age*, young people are certainly predisposed, especially to round-celled growths. The age at onset of symptoms works out in Stirling's and in Silcock's and Marshall's cases thus:

	Stirling.	Silcock and Marshall.
0—10	9	1
11—20	6	0
21—30	2	3
31—40	2	2
41—50	4	2
51—60	4	0
61—75	2	0
	—	—
	29	8

There is no evidence of *sex* predisposition (Stirling 14 male, 15 female; Silcock and Marshall 7 male, 2 female). *Hereditary* influence is not marked, and traumatism, not infrequently recorded—Hay, Verrall, Stirling (5 out of 29)—is probably of no ætiological moment.

The *duration* of the disease before operation in Stirling's cases varied from three weeks (round-celled) to eight years (osteo-sarcoma); another osteo-sarcoma was present for six years, and a spindle-celled growth for four years. The "osteo-sarcomata" were probably simple osteomata, though true osteo-sarcoma may be derived from the periosteum.

Recurrence occurred in seventeen of Stirling's twenty-nine tumours, the average time for twenty-eight being eight months. Recurrence took place in nine out of ten cases treated by excision of the growth, and in nine out of sixteen treated by exenteration of the orbit. The cases with recurrence were fourteen round-celled, four mixed round and oval, one mixed spindle and oval, eight spindle-celled. In four cases the primary tumour was composed of round, the recurrent of spindle cells.

Metastasis occurs early in the round-celled growths, later in the fibro-sarcomata; many of these are probably endotheliomata, which often show local malignancy only. Extension to the cranial cavity and periorbital sinuses occurs rapidly. Metastasis takes place *viâ* the blood-stream.

*STIRLING.—R. L. O. H. Rep., xiii, 1893. *SILCOCK AND MARSHALL.—R. L. O. H. Rep., xv, 1899. HAY.—Ann. d'Oc., xcix, 1878. VERRALL.—Brit. Med. J., 1893.

There is no predilection as to *side affected* (Stirling 13 right, 15 left; Silcock and Marshall 4 right, 5 left). The sarcomata, like the lymphomata, are sometimes *symmetrical* (Birch-Hirschfeld). Such cases have been reported by de Vincentiis (endothelioma), Zit (periosteal sarcoma, invading the opposite orbit *viâ* the lesser wing of the sphenoid), Rosmini (primary dural), Alt (angio-sarcoma), van Duyse (endothelioma), Davis (round-celled), Alexander (angio-sarcoma, secondary from cranial cavity), Colucci (round-celled), van der Straeten (round-celled), Löwi (fibro-sarcoma), Pagenstecher (from ethmoid), Nieden (from nose), Snell (round-celled), Snellen (fibro-sarcoma), de Schweinitz and Meiggs (round-celled, with secondary choroidal tumour), Bull (myxo-sarcoma), Schech (glio-sarcoma). Many of these were secondary growths.

ALT.—Amer. Jl. of Ophth., 1893. VAN DUYSSE.—A. d'O., xv, 1895. ALEXANDER.—Med. Times and Gaz., 1884. COLUCCI.—Lav. della Clin. oc. di Napoli, v. VAN DER STRAETEN.—Ophth. Klinik, 1900. LÖWI.—C. f. A., xiv, 1890. PAGENSTECHER.—A. f. O., xv, 1, 1869. NIEDEN.—A. f. A., xvi, 1886. SNELL.—T. O. S., xiv, 1894. SNELLEN.—Ann. d'Oc., cxvii, 1896. DE SCHWEINITZ AND MEIGGS.—Amer. Jl. of Ophth., 1894. BULL.—New York Med. Jl., 1893. SCHECH.—Münch. med. Woch., 1898. PAGENSTECHER.—A. f. O., liv, 2, 1904. *BIRCH-HIRSCHFELD.—A. f. O., lvi, 3, 1903.

Cytology.—Small round-celled sarcomata are relatively common, especially in young children, and very malignant, showing rapid growth and early dissemination (Noyes, Norris, Carmalt, Hirschberg and Birnbacher, Lawford, Snell, Beaumont, Valude, Polignani, Severi, Lagrange). They also contain spindle-shaped cells, and a fine fibrous reticulum. The early age strongly favours the probability of congenital deposits. These round-celled tumours are by no means always easy to diagnose histologically; the clinical history is of prime importance, and serious mistakes arise if this is neglected. The presence of an intercellular reticulum, and careful investigation of the cells by special staining methods, more particularly with a view to distinguishing them from lymphocytes, demand special attention. It is impossible in many cases to distinguish lymphomata, leukæmic tumours, etc., histologically from small round-celled sarcomata (*v. p.* 729). The same difficulty arises with regard to purely inflammatory swellings, especially gummata. Round-celled tumours of the orbit generally spring from the periosteum; hence they may contain osteoblasts, and give rise to osteo-sarcomata (Lagrange). I have described a typical myeloid or giant-celled sarcoma of the orbit, which also contained spicules of bone (Flemming and Parsons). Macroscopically the tumour was dark red, owing to hæmorrhages, and contained a cyst; microscopically it was found to contain very numerous giant cells.

The so-called glio-sarcomata belong to the small round-celled group; they are probably all either true round-celled sarcomata or secondary gliomata from the retina.

NOYES.—T. Amer. O. S., 1879. NORRIS.—New York Med. Jl., 1884. CARMALT.—T. Amer. O. S., 1885. HIRSCHBERG AND BIRNBACHER.—C. f. A., x, 1886. LAWFORD.—R. L. O. H. Rep., xii, 1888. SNELL.—T. O. S., xiv, 1894. BEAUMONT.—Ann d'Oc., cxv, 1896. VALUDE.—Soc. franç. d'O., 1898. POLIGNANI.—In Lagrange. SEVERI.—Ann. di Ott., xxxi, 1902. LAGRANGE.—Tumeurs de l'Œil, ii, 1904. KNAPP.—T. Am. O. S., 1896. FRANK.—New York Med. Record, 1904. FLEMMING AND PARSONS.—T. O. S., xxv, 1905.

The so-called fibro-sarcomata form a large section of the reported cases; they probably include a variety of conditions, especially inflammatory hyperplasias and endotheliomata. This view is supported by the fact that they are relatively benign, give rise to metastasis late or not at all, and may be cured by extirpation. They consist of spindle-shaped and round cells, lying in whorls and masses of fibrous tissue. The remarks made on primary extra-dural tumours of the optic nerve (p. 709) apply with equal force to many of these growths.

Besch has collected 15 cases of orbital sarcoma with cysts, which

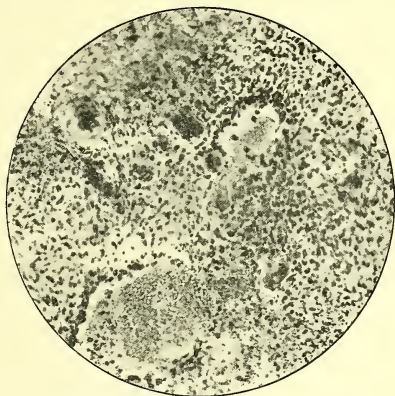


FIG. 533.—MYELOID SARCOMA OF THE ORBIT.
Flemming and Parsons, T. O. S., xxv.

contained clear or blood-stained fluid; he gives *résumés* of the anatomical conditions in the 12 cases in which these were examined (Singer, Sichel, Rémy, Vossius, Elschning, Walter, Juler, Hartridge, Kalt (2 cases), Knapp, Besch).

O'FERRAL.—Dublin Hosp. Gaz., ii, 1848. SICHEL.—Ann. d'Oc., 1865. LAWSON.—R. L. O. H. Rep., vi, 1868. ELLIOT.—Lancet, 1893. WHITE.—Jl. Amer. Med. Assoc., 1893. HOLDEN.—A. of O., xxii, 1893. KALT.—Soc. franç. d'O., 1895. SNELLEN.—Ann. d'Oc., cxvii, 1896. WILSON.—T. Amer. O. S., 1898. VEASEY.—T. Am. O. S., 1902. SILCOCK AND MARSHALL.—R. L. O. H. Rep., xv, 1903. WALTER.—K. M. f. A., xxxii, 1894. JULER.—Ophth. Rev., xvii, 1898. HARTRIDGE.—Ophth. Rev., xviii, 1899. KNAPP.—Internat. Congress, Utrecht, 1900. KALT.—Ann. d'Oc., cxxvii, 1902. *BESCH.—K. M. f. A., xlii, 1904.

Pigmentation.—Melanotic sarcomata of the orbit are usually secondary extensions from the choroid or conjunctiva. There is a small group of cases in which they are primary, though the difficulties attendant upon deciding the point will be readily appreciated. Melanotic tumours of the orbit are relatively benign (Desmarres, Sichel, Lagrange); in 11 cases collected by Lagrange 6 were benign,

recurrence occurred in 3, and the result was unknown in 4. The explanation given is that the pigment is invariably hæmatogenous; if this is so, they are not true melanotic sarcomata.

BUISSON.—Arch. gén. de Méd., 1852. LIGHTFOOT.—Med. Times and Gaz., 1852. LAWRENCE.—Tr. Path. Soc., 1886. SICHEL.—Ann. d'Oc., lix-lx, 1868. LEBERT.—Traité d'Anat. path. gén., i. GIRALDÈS.—In Demarquay, Tumeurs de l'Orbite, Paris, 1860. BENNETT.—Dublin J. of Med. Sc., 1880. DUFAIL.—Thèse, Paris, 1882. GAYET.—Ann. d'Oc., cxvii-cxviii, 1897. ACHENBACH.—Virchow's Arch., cxliii, 1896. WILLIAMS.—T. O. S., xvii, 1897. POLIGNANI.—In Lagrange, Tumeurs de l'Œil, ii, Paris, 1904.

Structure.—Whilst the sarcomata already mentioned—round-celled, spindle-celled, etc.—are marked by a tendency to infiltrate the surrounding tissues, and have no individual elaborated architecture, others

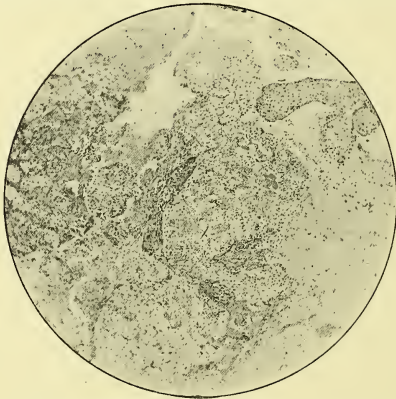


FIG. 534.—ENDOTHELIOMA OF THE ORBIT. $\times 55$.

The growth consists of a coarse network of large epithelioid cells, with large oval nuclei, each with a prominent nucleolus. Fibrous trabeculae separate the columns.

are characterised by a definite structure. To these belong especially the tumours hitherto described as angio-sarcomata. Here the neo-plastic cells are closely related to vessels, either blood-vessels or lymphatics, so that columns of cells are arranged in a coarse network. These tumours have hence been called plexiform sarcomata, cylindromata, alveolar sarcomata, or from a superficial resemblance to carcinoma, sarcoma carcinomatoides. There can be little doubt that most of these are caused by the malignant proliferation of endothelium; hence they have in recent years been termed endotheliomata (Golgi). It is probable that many of the so-called fibro-sarcomata of the orbit also belong histogenetically to the endotheliomata (*v.* p. 741). The subject of endothelioma has already been discussed in dealing with tumours of the choroid (p. 520). It is, therefore, only necessary to consider their special characteristics when present in the orbit.

Cylindromata were early recognised as most common in the neighbourhood of the eye (v. Graefe); local malignancy, but absence of generalisation, were also noted (Sattler). These observations have been confirmed by later reports (Billroth, van Duyse), but stress must be laid upon their infiltrating tendencies, resulting in the destruction of the surrounding tissues, and frequently in death of the patient (van Duyse, Kolaczek). When metastasis occurs it is by way of the blood-channels; considering that some of these endotheliomata spring from the lymphatics, it is surprising that the glands are not more often affected (van Duyse), but this has only rarely been observed (Tourman, van Duyse).

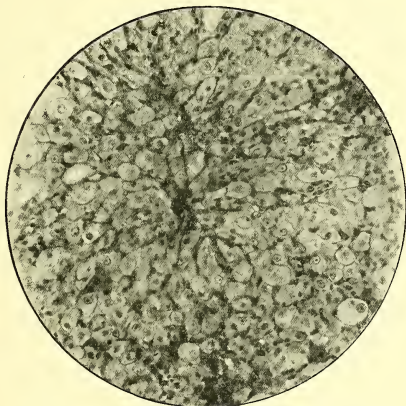


FIG. 535.—PERITHELIOMA OF THE ORBIT. $\times 220$.

The section shows a small vessel in the centre, surrounded by radiating columns of large endothelial cells. Stained by van Gieson's method. (See Snell, T. O. S., xxii.)

The cylindrical, plexiform (Alexander, Czerny), or quasi-alveolar structure is easily deducible from the near relationship of the growths to blood-vessels or lymphatics. The cells are usually well marked off from the connective-tissue stroma, the amount of which varies greatly. In the most typical parts the cells are distinctly endothelial in type, but every transition to spindle and branched cells is seen; hence the difficulty in diagnosis. Only the original sites of proliferation are absolutely pathognomonic; even the actively growing edges may show metaplastic variations which obscure the true origin of the cells. Lymphatic spaces lined or filled with endothelial cells display a remarkable similarity to carcinoma (Fig. 536), so that confusion has arisen from this cause.

The interference with the lymph flow in the orbit often causes

œdematous changes, which have given rise to the so-called myxo-sarcomata. Whether true myxo-sarcomata occur is uncertain, and can only be proved by the demonstration of mucin by chemical tests. Vacuolation is common in the cells and hyaline changes are often a marked feature, especially in the cylindromata; they are characteristic of endotheliomata in other parts of the body.

V. GRAEFE.—A. f. O., x, 1, 1864. SATTLER.—Ueber die sogenannten Cylindrome, 1874. BILLROTH.—Chir. Klinik, Wien, 1870-76. *VAN DUYSSE.—A. d'O., xv, 1895. KOLACZEK.—Deutsche Zeitschr. f. Chir., ix, xiii. ALEXANDER.—K. M. f. A., xii, 1874. CZERNY.—Langenbeck's Arch., xi. VEASEY.—T. Am. O. S., 1902. SNELL.—T. O. S., xxii, 1902. BENSON AND SYMES.—Med. Press and Circular, 1903.



FIG. 536.—ENDOTHELIOMA OF THE ORBIT. $\times 120$.
The growth closely resembles a scirrhous carcinoma.

Myxo-sarcomata have been described in the orbit by Lebert, Jacobson and v. Recklinghausen, Horner, Quaglino and Manfredi, Valerani, Novak, Letulle, Bull, Landsberg, and Norris. Of these ten cases, four were children under 10, three between 20 and 30, one 55, and one 67. The cases of Horner, Letulle, Novak, and Norris recurred rapidly after removal. As already stated, these tumours are probably œdematous sarcomata.

LEBERT.—Virchow's Arch., iv, 1852. JACOBSON AND V. RECKLINGHAUSEN.—A. f. O., x, 2, 1864. HORNER.—K. M. f. A., viii, 1871. QUAGLINO AND MANFREDI, VALERANI.—Ann. di Ott., iii, 1873. NOVAK.—Wiener med. Presse, 1877. LETULLE.—Soc. anat. de Paris, 1877. BULL.—Med. Record, 1879. LANDSBERG.—Virchow's Arch., lxiii. NORRIS.—New York Med. Jl., 1884. BULL.—T. Am. O. S., 1898. JULER.—T. O. S., xix, 1899. FEJÉR.—A. f. A., xliv, 1902.

Chondro-sarcoma in the orbit is rare. Two cases mentioned by Mackenzie were not examined microscopically; three by Fano,

Fromaget, and Paul rest upon histological evidence. Probably these were tumours of the lacrymal gland (*v. infra*), like the mixed tumours of the parotid, or congenital tumours.

FANO.—Union méd., iii, 1859. FROMAGET.—Soc. de Méd. et de Chir. de Bordeaux, 1902. PAUL.—Brit. Med. J., 1902.

Myo-sarcoma.—Four cases of rhabdomyoma (Bayer, Zenker, Jennings, Bocchi) and one of leiomyoma (Lodato) have been described in the orbit. Bocchi's case was probably a fibroma of the superior rectus, the striped muscle-fibres being normal preformed ones. The other 3 rhabdomyomata occurred in young children (æt. 3, 7, and 1 years), and were probably genuine congenital neoplasms. The cases of Bayer and Zenker are very carefully described. Lodato's case is doubtful.

BAYER.—Nord. med. Ark., xiv, 1882. ZENKER.—Virchow's Arch., cxx, 1890. JENNINGS.—Amer. J. of Ophth., 1895. BOCCHI.—Arch. di Ott., v, 1897. LODATO.—Arch. di Ott., iv, 1896.

Glio-sarcoma.—Two cases are described as glio-sarcoma by Lagrange, who seeks to support the thesis that glioma may arise in the orbit, independently of retinal growth, from congenital "rests." Both patients were infants, æt. 20 days and 3 years respectively.

LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904.

SECONDARY SARCOMATA.

Secondary sarcomata of the orbit are derived from primary growths in the uveal tract; their mode of propagation and histological characteristics have already been considered.

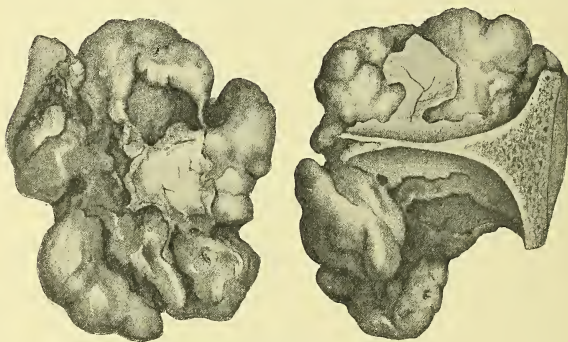
There is no evidence of metastatic deposits in the orbit from sarcomata in other parts of the body, with the possible exception of the obscure group of lympho-sarcomata.

OSTEOMA.

Osteomata, growing from the walls of the orbit, are so striking in their clinical peculiarities that most of those observed have probably been published. Lagrange has succeeded in collecting 148 cases, the earliest being attributed to Veiga (1506). A skull in the museum of the Royal College of Surgeons (No. 795) shows the condition, and is depicted by Baillie (1799); others follow, reported by Middlemore, Howship, Cooper and Travers, and Bell. Then follows the stage of operative interference, inaugurated by Salzer (1831); total extirpation was first attempted and successfully carried out by Canton (1851). Many similarly successful results were recorded until 1865, when Knapp lost two cases from meningitis; unfortunately, many of the tumours spring from the cranial walls of the orbit, considerably increasing the danger of surgical interference.

Analysis of Lagrange's 148 cases shows that the disease commences in early life. The data for precise time of onset are wanting, but taking the ages as given, modified when the duration is definitely stated, the average age works out at 27 years; there can be no doubt that this is far above the true age of onset in most cases; probably the growth starts at the time of ossification of the orbital bones. Exceptional cases may be due to ossifying periostitis. The sex is stated in 121 cases, 63 being male and 58 female.

Osteomata of the orbit are rounded tumours, with a smooth but knobby surface (Figs. 537, 538). They vary in size from a pea to an orange: Walton's case is notorious from the size of both tumours, the disease having been bilateral. Usually only one side is affected; when both are involved, it is nearly always due to a single tumour. Howship's



FIGS. 537, 538.—EXOSTOSIS OF THE ORBIT.

Tweedy, R. L. O. H. Rep., x. Natural size.

case is an exception, and Solger found several ivory osteomata in the two frontal sinuses at an autopsy. Only one tumour too is present in the orbit affected; the cases of Tillmans and Tauber are exceptions. Though usually rounded, they may show evidence of being moulded to the cavity in which they grow, *e.g.* frontal sinus (Tauber). They may be distinctly lobulated (Weinlecher), heart-shaped (Michon), cubical (Jamain), finger-shaped (Weiss), etc. The largest orbital osteomata on record are those of Weinlecher (24 cm. in circumference, 281 gm.), Michon (20 cm. in circumference), Carreras Arago (587 gm.), Mitvalsky (180 gm.), Arnold (110 gm.), etc.

The tumour is generally sessile, with a large base; very rarely it is pedunculated, or even free in a sort of cystic cavity (Arnold, Dolbeau, Panas).

The growth may spring from any part of the orbital walls; it is, however, commonest at the upper and inner angle, near the frontal

sinus (21 out of 55 cases, Tchlinghiroff); next in frequency comes the floor (17 cases), then the roof (13 cases). Lagrange's statistics give 40 per cent. upper and inner angle, 30 per cent. inner wall, 1 per cent. floor, and 0.5 per cent. outer angle. They often arise in connection with the sinuses, either frontal or ethmoidal, rarely the antrum of Highmore (2 cases, Tchlinghiroff). Secondary extension from the cranial cavity is rare (Fergusson, Pareja, Tweedy, Mitvalsky); it is difficult to decide whether the orbital or the intra-cranial growth is primary, both being slow and insidious.

Osteomata grow very slowly; out of 37 cases in which the apparent commencement is noted, growth occupied 1 to 5 years in 27, 5 to ten years in 7, 10 to 20 years in 2 (Sporing, Busch), 42 years in 1 (Imre). Spongy osteomata grow more rapidly than the ivory type.

Inflammation often occurs around the tumour, and may lead to permanent fistulæ; the growth has been known to become detached and pass out through such a fistula (Lediard, Strachow).

Most of the orbital osteomata are of the intensely hard, compact, ivory type (70 per cent., Lagrange); others are spongy (12 per cent.); others again are cystic, semi-cartilaginous, etc. The ivory exostoses consist of dense, concentric layers of compact bone, devoid of blood-vessels (Virchow). The inner parts are sometimes spongy, but this is rare. Spongy osteomata may contain cartilage, and do not always possess a compact covering. Rokitansky regarded osteomata of the frontal sinus as ossifying enchondromata, but this view has not been generally accepted. The purely orbital growths are covered by a simple layer of periosteum; those arising in the sinus have a covering of mucous membrane. The latter consists of stratified epithelium separated from the periosteum by a layer of connective tissue. There are often polypoid excrescences upon the surface, formed from the mucous membrane; the epithelium may be ciliated (Mitvalsky), and lymphoid aggregations are not uncommon. Cystic spaces may also be formed in the mucosa in these tumours (Coppez).

VEIGA.—In Schenck, *Observationum medicarum libri septem*, Frankfort, 1665. BAILLIE.—Series of Engravings, London, 1799. MIDDLEMORE.—Diseases of the Eye, London, 1835. HOWSHIP.—Practical Observations in Surgery, London, 1816. COOPER AND TRAVERS.—Surgical Essays, London, 1818. BELL.—Diseases of the Bones, Glas. Med. Jl., 1828. SALZER.—Lancet, 1831. HILTON.—Guy's Hosp. Rep., 1836. MICHON.—Soc. de Chir., 1851. CANTON.—Med. Times, xxiii, 1851. PAGET.—Lectures, ii, 1853. WALTON.—Operative Ophth. Surgery, London, 1853. BADER.—R. L. O. H. Rep., iii, 1860. KNAPP.—A. f. O., viii, 1865; K. M. f. A., iii, 1865; A. f. A., xi, 1882. FERGUSSON.—Tr. Path. Soc., 1868. ARNOLD.—Virchow's Arch., lviii, 1870. WEINLECHER.—Wiener med. Blätter, 1883. CARRERAS-ARAGO.—Rec. d'O., 1881. IMRE.—C. f. A., vi, 1882. LEDIARD.—T. O. S., iii, 1883. TWEEDY.—R. L. O. H. Rep., x, 1883. ANDREWS.—Med. Record, 1887; Ophth. Rev., vi, 1887. SILCOCK.—T. O. S., viii, 1888; xii, 1892. SNELL.—T. O. S., x, 1890. BEAUMONT.—T. O. S., xii, 1892. SNELL, COLLIER GREEN.—T. O. S., xiv, 1894. MITVALSKY.—A. d'O., xiv, 1894. COPPEZ.—A. d'O., xv, 1895. GRIFFITH.—T. O. S., xxi, 1901. FRIEDENBERG.—T. Am. O. S., 1903. BROWNE.—Soc. franç. d'O., 1903. *LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904 (Bibliography). BIRCH-HIRSCHFELD.—K. M. f. A., xlii, 1904.

TUMOURS INVOLVING THE WALLS OF THE ORBIT SECONDARILY

Tumours of the frontal sinus.—Apart from chronic empyema of the frontal sinus, which can only be mentioned here, cysts are occasionally found. These are usually of inflammatory origin—obstruction of the

infundibulum, cysts of the mucous membrane, etc. True tumours include mucous and fibrous polypi, which dilate the cavity and lead to absorption of the walls, osteomata, which have already been considered (p. 747), and malignant growths. Most of the latter which have been described have been osteo-sarcomata (Stroppa, Kundrat, Trombetta, Bergé) or simple sarcomata (Martin—fibro-sarcoma, Hérold—endothelioma, Bergé); epitheliomata and carcinomata may also occur (Brian, Hellmann).

LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904. STROPPA.—Ann. di Ott., ix, 1880. KUNDRAT.—Wiener med. Jahrb., 1883. TROMBETTA.—Ann. di Ott., xxx, 1901. BERGÉ.—Thèse, Lyon, 1902. MARTIN.—Thèse, Paris, 1887. HÉROLD.—Inaug. Diss., Würzburg, 1889. BRIAN.—Lyon médicale, 1896. HELLMAN.—Arch. f. Laryng. und Rhinol., vi, 1897. AXENFELD.—K. M. f. A., xlii, 1904.

Tumours of the ethmoid.—Mucocèles, like those of the frontal sinus, have been met with (Hötz, Masse); osteomata have been referred to elsewhere (p. 747). Malignant tumours are sarcomata (Flower, Vohsen, Auvret and Pilliet, van Duyse), psammomata (Burnett, Badal), and carcinomata, including epitheliomata (Sourdille, Harris), adenomata (Aubaret, Moure, Snell, Lagrange, Dundas Grant).

HÖTZ.—Jl. of the Amer. Med. Assoc., 1899. MASSE.—Soc. de Chir., 1903. FLOWER.—R. L. O. H. Rep., iv, 1865. VOHSEN.—Rev. de Laryngol., 1890. AUVRET AND PILLIET.—Soc. anat. de Paris, 1898. BURNETT.—Arch. of Otol., xxviii, 1899. BADAL.—In Lagrange. SOURDILLE.—Soc. anat. de Paris, 1896. HARRIS.—New York Acad. of Med., 1895. SNELL.—T. O. S., xvii, 1897. LAGRANGE.—Tumeurs de l'Œil, ii, 1904. DUNDAS GRANT.—Laryngol. Soc., 1900. *VAN DUYSE.—A. d'O., xxiv, 1904.

Tumours of the sphenoid.—Tumours of the sphenoid include polypi, enchondromata (Lawson), osteomata (Spencer Watson, Nettleship, Gallet and Coppez), sarcomata (Nieden, Behring and Wicherkiewicz), and carcinomata (Morax, Jocsq).

SPENCER WATSON.—Tr. Path. Soc., 1868. NETTLESHIP.—T. O. S., vii, 1887. GALLET AND COPPEZ.—A. d'O., xxi, 1901. NIEDEN.—A. f. A., xvi, 1886. BEHRING AND WICHERKIEWICZ.—Berliner klin. Woch., 1882. MORAX.—Ann. d'Oc., cxv, 1896. JOCSQ.—Soc. franç. d'Opht., 1896.

Cysts and tumours of the superior maxilla, etc., belong rather to the domain of general surgery, and will not be considered here.

CHAPTER XIII

THE LACRYMAL APPARATUS

THE NORMAL LACRYMAL APPARATUS

THE lacrymal apparatus consists of the lacrymal gland—using the term in its widest significance to include all lacrymal glandular tissue, *i. e.* the superior, inferior, and accessory (Krause's) lacrymal glands—the lacrymal ducts, the puncta, canaliculi, lacrymal sac, and the nasal duct.

The lacrymal gland.—The lacrymal gland proper consists of two parts—the superior or orbital gland and the inferior or palpebral gland. The ducts of the former pass through the latter, receiving many of its ducts, whilst others open independently into the fornix. The ducts seldom exceed twelve in number.

Both parts of the lacrymal gland have the same structure, being serous glands exactly resembling serous salivary glands. They have been reconstructed from serial sections by Maziarski, who has shown that they are not acinous (Boll and others), nor tubulo-acinous (*v. Kolliker*), but tubular. Axenfeld has shown that in the new-born child they contain no adenoid tissue. In the adult, on the other hand, they contain a large quantity of adenoid tissue between the gland tubules. This is a matter of considerable pathological importance, rendering the diagnosis of inflammatory conditions exceptionally difficult.

The gland tubules, which have no half-moon cells of Gianuzzi such as are found in salivary glands, show similar changes as the result of secretory activity (*Schäfer, Noll*).

There is considerable doubt as to the exact innervation of the lacrymal gland. Though supplied by the fifth cranial nerve, it is probable that the actual fibres come from the seventh or facial trunk, being ultimately derived from the nucleus of the glossopharyngeal (*see Parsons*).

The ducts are lined with a double layer of epithelium, the inner layer being cubical, the outer flattened.

The puncta and canaliculi.—The puncta are situated on a slight elevation which is normally in contact with the bulbar conjunctiva.

The elevation is least in young people, and may be very considerable in the aged. In longitudinal section the puncta are triangular, the apex being the narrowest part.

From the puncta the canaliculi pass for about 1.5 mm. upwards or downwards, as the case may be, and then turn sharply inwards to run for 10 mm. to their termination in the lacrymal sac. They usually open separately into the sac, occasionally by a common aperture (14 per cent. of cases, Huschke).

The canaliculi are lined by stratified epithelium, composed of six to twelve layers and reaching a thickness of 60 to 100 μ . It is doubtful if there is a true basement membrane. There is an extraordinary amount of elastic tissue around the puncta (Halben); outside this the fibres of the orbicularis palpebrarum form a definite sphincter.

The canaliculi open into the posterior surface of the sac at about the level of the internal palpebral ligament or slightly higher. The last 1-3 mm. of the canaliculi may show the characters of structure of the sac—cylindrical epithelium, adenoid layer, and absence of muscular coat—but this appears to be inconstant (Schirmer).

The lacrymal sac.—The lacrymal sac is about 12 mm. long—varying from 10 to 24 mm.—and 15 mm. in diameter (Merkel). It is lined by cylindrical epithelium, usually in two layers, the inner layer consisting of very high cells (35-50 μ); there is a definite basement membrane. It is doubtful whether the cells ever bear cilia. There are often many goblet cells.

Beneath the basement membrane is an adenoid layer of the usual type; it is doubtful if it ever contains follicles normally (Hertel, Tartuferi).

The submucosa consists of dense fibrous tissue, which is very vascular, especially on the parts adjacent to the bone. There is no muscular coat, but elastic fibres are abundant, mostly in the anterior part above the palpebral ligament. Small serous glands, resembling sweat-glands, are occasionally present in the submucosa, especially at the fundus of the sac (8 per cent. of cases, Joeress).

The nasal duct.—The nasal duct varies much in length (12-24 mm.) and somewhat in diameter (3-4 mm.); the lumen both of the sac and of the duct is a mere capillary cleft during life.

The duct is lined by two or more layers of high cylindrical cells, which in the fœtus bear cilia (Stanculéanu). There are many goblet cells. The mucosa consists of adenoid tissue, and the submucosa of dense fibrous tissue containing many vessels, chiefly veins. There are no muscular and but few elastic elements.

The upper end of the duct is the narrowest part, and there is often here a considerable thickening of the walls, which is a fact of some pathological importance.

MAZIARSKI.—Anat. Hefte, lviii, 1901. SCHÄFER.—In Quain's Anatomy, iii, 3, 1894. NOLL.—Arch. f. mikr. Anat., lviii, 1901. PARSONS.—R. L. O. H. Rep., xv, 1902. HALBEN.—A. f. O., lvii, 1, 1903. HERTEL.—A. f. O., xlviii, 1899. TARTUFERI.—A. d'O., xxii, 1902. JOERESS.—B. z. A., iii, 1898. ROCHON-DUVIGNEAUD.—A. d'O., xix, 1899, xx, 1900. STANCULÉANU.—A. d'O., xx, 1900. *SCHIRMER.—A. f. O., lvi, 2, 1903; in G.-S., 1904.

CYSTS OF THE LACRYMAL GLAND

Cysts of the lacrymal gland, though long recognised, are rare. They are usually described as *dacryops*, a term introduced by Schmidt (1803). Beer reported six cases, rightly regarding them as retention cysts; he carefully examined the fistulæ which sometimes result from the condition. Other cases were described by Jarjavray (1853), Bowman (1858), von Graefe (1860), de Wecker (1867), and others. Polaillon in 1868 reviewed the previously published cases, and in 1896 Francke wrote an important monograph on the subject; zur Nedden in 1903 collected thirty-three reported cases.

Lagrange divides the cases into (1) cysts of the accessory (*i.e.* the inferior) lacrymal gland, including (*a*) simple dacryops, and (*b*) fistulous dacryops; and (2) cysts of the lacrymal gland proper (*i.e.* the superior or orbital gland). Most cases belong to group 1a (Walton, Jarjavray, Broca, de Wecker, Ilken, Francke, Lawson, Sourdille, Lange, Lagrange, and others). Schmidt, Bowman, Jarjavray, v. Graefe, and Arlt described



FIG. 539.—DACRYOPS.

After Lawson.

cases of fistulous dacryops. Cysts of the orbital gland are all open to doubt as to their true pathology (Spry, Schmidt, Forster, Cosse).

Cysts of the inferior lacrymal gland—dacryops proper—are rounded, more or less transparent, superficial swellings, situated at the outer angle of the upper *cul de sac*. They may be flattened (Fráncke), or lobulated (de Wecker). They vary in size from a pea to a pigeon's egg. The conjunctiva is freely movable over them. If sufficiently large, fluctuation can be demonstrated, and the fluid can occasionally be pressed out through minute openings or through a definite fistula. Variations in volume of the same tumour may be noted occasionally.

Dacryops has been examined microscopically by Legros, Francke, Lagrange, Ahlström, and others. In Legros' case the cyst was lined with cylindrical epithelium resembling that of the lacrymal ducts. Francke also found a single layer of epithelial cells; he noted specially normal ducts which were constricted in places: similar structure was found by Lange and Rogman (2 cases). Lagrange found a single layer of cylindrical epithelium lining the cyst. Sourdille found a single or double layer of cubical epithelium, or flattened endothelioid cells lining different parts of the cyst; Ahlström's case was similar.

The fluid contained in the cysts is more or less altered lacrymal secretion, colourless, or in the older cysts slightly yellow; it has been analysed by Broca, and by Badal and Aubaret. It contains sodium chloride and proteid material, with traces of sulphates and fats: cholesterin, epithelial cells, and leucocytes—mostly polymorphonuclears—may also be present: there is no mucin.

These data tend to show that the cases examined were retention-cysts. The cause is usually some injury involving the ducts, *e. g.* incomplete extirpation of a dermoid (Beer), a burn (Broca). Francke considers that there is inflammatory sclerosis around the ducts. It is possible that there may be an ascending infection from the conjunctiva (Sourdille), but in Badal and Aubaret's case the contents were sterile.

Cysts of the orbital gland are probably due to definite neoplasms (*v. infra*).

It is a curious fact that concretions, similar to those found in the salivary glands, have not been observed in relation with dacryops. They are, indeed, rare, but a case has been reported in connection with an otherwise normal lacrymal gland by Levi.

SCHMIDT.—Ueber die Krankheiten des Thränenorgans, Wien, 1803. BEER.—Lehrbuch der Augenkrankheiten, Wien, 1817. JARJAVRAY.—Mém. de la Soc. de Chir., iii, 1853. BOWMAN.—R. L. O. H. Rep., i, 1858. v. GRAEFE.—A. f. O., vii, 2, 1860. DE WEEKER.—Gaz. hebdom., 1867. POLAILLON.—Dict. encycl. des Sc. méd., 1868. *FRANCKE.—A. f. O., xlii, 1, 1896. *LAGRANGE.—Tumeurs de l'Œil, ii, Paris, 1904. WALTON.—Med. Times and Gaz., 1854. BROCA.—Ann. d'Œc., xlv, 1861. ILKEN.—Lancet, 1867. LAWSON.—T. O. S., xvii, 1897. SOURDILLE.—Soc. franç. d'Ophth., 1899. LANGE.—A. f. O., xlvii, 3, 1899. SPRY.—In Mackenzie, Diseases of the Eye. FORSTER.—A. of O., xx, 1891. COSSE.—Soc. franç. d'Ophth., 1903. LEGROS.—In Dubrueil, Gaz. des Hôp., 1870. BADAL AND AUBARET.—Jl. de Méd. de Bordeaux, 1902. ZUR NEDDEN.—K. M. f. A., xli, 1903. *AHLSTRÖM.—K. M. f. A., xlii, 1904. LEVI.—K. M. f. A., xli, 1903, Beilageheft.

TUMOURS OF THE LACRYMAL GLAND

Tumours originating in the lacrymal gland are relatively uncommon; Warthin (1901) collected 132 cases. It is impossible to arrange these accurately according to their true pathology, owing partly to the inadequateness of many of the descriptions, but more especially to the change in our conception of morbid growths. Many were described as simple hypertrophy, adenoma, cancer, or by complex terms enumerating the elementary constituents. There is a growing tendency to consider epithelial growths of the lacrymal gland rare, the great majority of the neoplasms being of endothelial origin. The particular type of endothelioma is almost identical with the well-known mixed growths of the parotid and other salivary glands, these being now generally regarded as endothelial. When the identity in structure of the lacrymal gland with a serous salivary gland is considered, the former being only physiologically differentiated from the latter, it is not surprising that both organs should be subject to identical morbid processes. This is seen in the dacryoadenitis occasionally accompanying parotitis, and it is further manifested in the new growths arising in the glands.

The first lacrymal gland tumours were described as scirrhus—Démours (1741), Boerhave (1749), Warner (1752), Himly (1807),

Guérin (1808). This diagnosis was contested by Schmidt, Velpeau, Mackenzie, and others, to be again revived by Beer (1817). Scirrhus and hypertrophy held the field almost unchallenged for the next fifty years, the latter being reported by Pemberton (1847), Busch (1854), Wharton-Jones (1864), and Rothmund and Letenneur (1865). The terms "adenoid" and "cancroid" then became common—Knapp (1865), Becker (1867), Adams (1870). Sarcoma was diagnosed by Stengel (1866), Emmert (1870), Alexander (1874), Nettleship (1875). Sautereau reported a myxoma in 1870, Butlin a "rare case of enchondroma" (1875), and after this time adenoma and complex descriptive terms became prevalent. It is only recently that any real attempt has been made to grasp the true pathogenesis of these tumours, notably by Warthin (1901).

The chaotic condition of the terminology of lacrymal growths is well exemplified by the analysis of the 132 cases collected by Warthin. Grouping these according to the diagnosis given by the original observer, they fall into the following pathological classes:

Hypertrophy	13	Chloroma	3
Fibroma	4	Leukæmic tumour	1
Fibroplastique	1	Lymphadenoma	2
Fibrolipoma	1	Lymphoma	3
Fibrochondroadenoma	1	Lymphadenosarcoma	1
Fibroadenoma	1	Lymphatic hypertrophy	1
Myxoma	1	Myxosarcoma	1
Myxochondroma	2	Myxoadenosarcoma	1
Myxoadenoma	2	Adenoid	2
Chondroma	4	Adenoma	13
Chondroadenoma	1	Adenoma with cancroid	1
Angioma	2	Cancroid	1
Sarcoma	14	Carcinoma	6
Round-celled sarcoma	7	Scirrhus	13
Spindle-celled sarcoma	2	Medullary cancer	2
Adenosarcoma	2	Encephaloid cancer	1
Fibrosarcoma	1	Epithelioma	1
Cylindroma	1	Glandular cancer	1
Colloid epithelioma	1	Symmetrical swelling	1
Secondary cancer	1	Enlargement	1
Myxoadenocarcinoma	1	Fibroid hyperplasia	1
Enchon. myx. carcinomatodes	2	Undiagnosed	5
Cysts	3		—
Dermoid cysts	1	Total	132

Warthin points out that more than two thirds of the neoplasms in this list are of mesoblastic origin; moreover, many set down as scirrhus were not examined microscopically.

The first microscopical examination of a lacrymal growth was made by Becker (1867); this he described as an overgrowth of both glandular and interstitial elements, the former being designated "adenoid" or adenomatous, the latter "cancroid" or fibromatous. Köster, in a

critical review of Becker's and Busch's cases, concluded that they were cylindromata arising from the proliferation of the endothelium lining the lymph-spaces. Berlin accepted this view and placed the cases of Todd, O'Beirne, Bérard, Lawrence, de Vincentiis, and Butlin in the same class. This work of Köster and Berlin seems to have attracted little attention, only one case being described as a cylindroma, and none as endothelioma. There can be little doubt that all the cases in

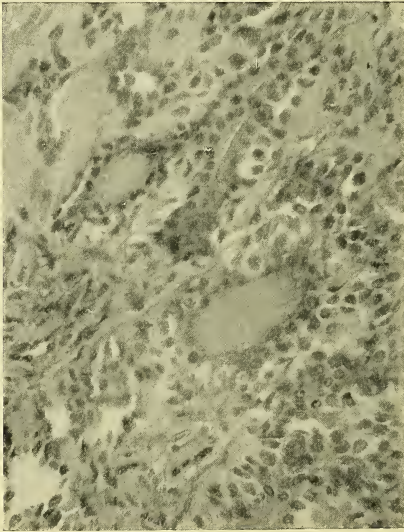


FIG. 540.—ENDOTHELIOMA OF THE LACRYMAL GLAND.

A. Hugh Thomson, T. O. S., xxii. Showing the alveolar arrangement of the cells and spaces containing hyaline material. The growth was probably of the same type as the mixed tumours of the parotid gland.

which cartilage, hyaline, and myxomatous tissue were present in the growth are similar or identical with the mixed tumours of the parotid. Such cases as the sarcoma carcinomatodes with mucoid change (Werner), adenochondroma (Figos), the cases of Alt, etc., were certainly of this nature. The high proportion—5 out of 7—of Alt's cases with cartilaginous and myxomatous constituents is very significant, especially when the proportion they bear to the total number of reported lacrimal tumours is considered.

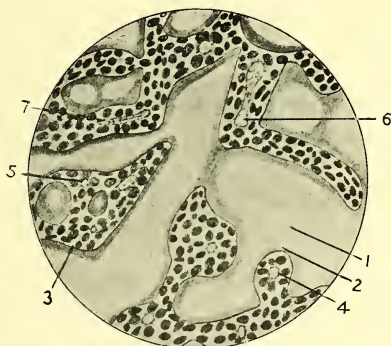


FIG. 541.—MIXED TUMOUR OF THE LACRYMAL GLAND. Zeiss obj. DD, oc. 4.

Verhoeff, JI. of Med. Research, xiii. Cylindromatous area. 1. Degenerated stroma. 2. Basement membrane of connective tissue. 3. Fibroglia membrane. 4, 5. Glandular lumina in transverse section. 6, 7. Lumina in longitudinal section.



FIG. 542.—MIXED TUMOUR OF THE LACRYMAL GLAND. Zeiss obj. $\frac{1}{3}$, oc. 4.

From the same specimen. Gland-formation in a tissue-space. The internal fenestrated membrane is seen in plane section, showing it to be composed of hexagonal loops, each enclosing a double dot. The sharp dotted line at the periphery of the gland represents Mallory's fibroglia membrane. Stained with phosphotungstic acid hæmatoxylin.



FIG. 543.—MIXED TUMOUR OF THE LACRYMAL GLAND. $\times 110$.

From the same specimen. Glandular acini invading nerve.

Simultaneous occurrence of tumours of the lacrymal and salivary glands has been frequently reported (Snell, Fuchs, Haltenoff, Mikulicz, de Wecker, and others).

These serous gland endotheliomata all occur usually in early adult life, form painless tumours of slow growth, are generally encapsuled, produce pressure effects chiefly, show little tendency to recur, and rarely become malignant. It must be remembered, however, that in rare cases they do take on malignant proliferation. They arise from the flattened endothelium of the lymph spaces, but the cells rapidly become unrecognisable as endothelial cells, showing very marked metaplastic tendencies, with the development of cartilage and degeneration into hyaline or myxomatous tissue. The researches of v. Ohlen, Kelly, and others on the salivary growths place the origin of the cells almost



FIG. 544.—MIXED TUMOUR OF THE LACRYMAL GLAND. Zeiss obj. $\frac{1}{12}$, oc. 4.

From the same specimen. Glandular formation in stroma, showing spiral fibril. The lines running towards the lumen, which contains colloid secretion, are vertical bars of the fenestrated membrane. Stained with phosphotungstic acid hæmatoxylin.

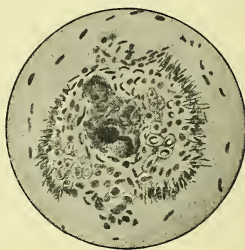


FIG. 545.—MIXED TUMOUR OF THE LACRYMAL GLAND.

Verhoeff, JI. of Med. Research, xiii. Alveolus containing an epithelial pearl. Numerous spiral fibrils are seen running between the basal cells; prickly cells and kerato-hyalin granules are also present. Stained with phosphotungstic acid hæmatoxylin.

beyond doubt, but confusion is liable to arise from the term "endothelioma" because these growths differ wholly from the more malignant types of endothelioma found elsewhere, *e.g.* in the choroid; endotheliomata of the orbit, optic nerve sheath, &c., would seem to occupy an intermediate position.

As might be expected, the endothelial origin of these tumours has not been universally accepted; the epithelial origin of the salivary gland growths has been voiced by Wood,¹ that of the lacrymal ones by Verhoeff. The reasons brought forward by the latter are: (1) The close connection of the tumours with the lacrymal gland, an essentially epithelial structure; (2) the presence in the parenchyma of gland-like lumina, whose lining cells show a fenestrated internal membrane and double dots in the centres of their inner ends; (3) the presence of a basement membrane of connective tissue beneath the marginal cells

¹ Wood.—Annals of Surgery, 1904.

in the cylindromatous areas; (4) the occurrence of cell masses containing pearls, keratohyalin granules, and prickly cells; (5) the occasional presence of peculiar spiral fibrils between the cells of the parenchyma. The dots referred to were first described by Weigert in normal ependyma, where many occur in each cell, but in the embryo each cell contains only a double dot. Lewy,¹ who studied them in gliomata of the brain, concluded that they were centrosomes. The true glandular lumina are distinguished from mere stroma spaces by possessing a fenestrated membrane, and by the absence of Mallory's fibrogliia membrane.² The spiral fibrils were discovered by Herxheimer³ in normal skin stained by Weigert's fibrin method; they have been regarded as fibrin (Eddowes⁴), unequal shrinkage (Herxheimer and Müller⁵), and epithelial structures (Verhoeff). The occurrence of cartilage in the tumours is difficult to explain on the theory of an epiblastic origin.

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DACRYOCYSTITIS

Bacteriology.—Attention was drawn to the extraordinary number of bacteria in pus from the lacrymal sac by Schmidt-Rimpler, Sattler, Widmark, and others. Most of the earlier reports describe staphylococci and streptococci, whilst later pneumococci were found frequently and in virulent form (Gasparrini, Mazet, Cuénod, Uhthoff and Axenfeld). Since these often form chains in culture, it is probable that they were earlier frequently mistaken for streptococci (Axenfeld).

Streptococcus pyogenes is especially associated with phlegmonous dacryocystitis, and the pneumococcus with the simple type, though it is seldom found in pure culture. In a smaller number of cases Fried-

¹ LEWY.—*Virchow's Arch.*, clxxi, 1903.

² MALLORY.—*Jl. of Med. Research*, 1903.

³ HERXHEIMER.—*Arch. f. Derm. u. Syphilis*, xxi, 1889.

⁴ EDDOWES.—*Monatshefte f. Derm.*, xi, 1890.

⁵ HERXHEIMER AND MÜLLER.—*Arch. f. Derm.*, xxxvi, 1896.

länder's pneumobacillus or the so-called ozæna bacillus is found (Sattler, Terson and Gabriélidès, Mazet, Cuénod, Uhthoff and Axenfeld, Gourfein). It was expected that this organism would be a common cause of hypopyon ulcer (Terson and Gabriélidès, etc.), but this expectation has not been realised. It has been found in patients suffering from ozæna (Terson and Gabriélidès, Mazet, Lodato), but even in these cases hypopyon ulcer is usually due to pneumococci (Axenfeld).

The organisms more rarely found in purulent dacryocystitis have been the bacterium coli (Mircoli, Mazet, Uhthoff), bacillus pyocyaneus (Sattler), various unclassified bacilli (Sattler, Uhthoff, Mazet), sarcinæ, actinomyces albus (Ricchi).

Xerosis bacilli are common in non-purulent dacryocystitis (mucosele) (Fage), and may be present as a pure culture. The mucous secretion is by no means harmless; Cuénod found pneumococci in eight cases out of 10 examined.

In gangrenous "pericystitis" Veillon and Morax found the anaërobic bacillus funduliformis, another anaërobic bacillus, as well as streptococci.

Cases of rhinoscleroma have been reported by Gallenga, but are very rare; so too glands (Gourfein).

Dacryocystitis, not uncommon in the new-born, may be easily mistaken for ophthalmia neonatorum (Peters).

SCHMIDT-RIMPLER.—Berlin. klin. Woch., 1876. SATTLER.—B. d. o. G., 1885. WIDMARK.—Beiträge zur Ophth., Leipzig, 1891. GASPARRINI.—Ann. di Ott., xxii, 1893; xxiv, 1895. MAZET.—Ann. d'Oc., cxi, 1894; Thèse de Paris, 1895. CUÉNOD.—Congrès franç. d'Ophth., 1895. UHTHOFF AND AXENFELD.—A. f. O., xlii, 1, 1896; xlv, 1, 1897. TERSON AND GABRIÉLIDÈS.—A. d'O., xiv, 1894. *AXENFELD.—In Kolle and Wassermann, Handbuch d. path. Mikroorg., Jena, 1903. RICCHI.—Ann. di Ott., xxviii, 1899. FAGE.—Ann. d'Oc., cxv, 1896. VEILLON AND MORAX.—Ann. d'Oc., cxxiii, 1900. GALLENGA.—C. f. A., xxiii, 1899. GOURFEIN.—A. d'O., xviii, 1898. PETERS.—Z. f. A., ii, 1899. CIRINCIONE.—La Clinica oculistica, 1903.

CONCRETIONS IN THE CANALICULI

Concretions are occasionally met with in the canaliculi, almost invariably the lower one (36 out of 40 cases on record, Axenfeld). A slowly increasing swelling is noticed, rarely reaching the size of a hazel-nut; it is accompanied by slight redness and catarrh. On slitting up the canaliculus, a greenish or brown mass is seen, and is easily expressed, as it is not adherent to the walls. It is waxy or granular in appearance, and is very friable; in some cases it is gritty, containing calcareous salts (v. Graefe, Grüning).

The condition has long been known—Cesoni (1670), Sandifors (1779), Desmarres (1842). v. Graefe (1854) first gave a clear description, based on 10 cases. He asserted the organic nature of the deposits, and was inclined to identify them with favus. Cohnheim regarded them as leptothrix, such as is found in the mouth, and this opinion was supported by Leber and Waldeyer, although these observers recognised that the filaments were finer and sometimes branched. v. Graefe subsequently adopted the diagnosis leptothrix, and this term was used until Cohn (1878) pointed out the differences,

and introduced the name "*Streptothrix Foersteri*." The older literature was revised on this basis, which was found to be generally applicable (v. Reuss, Goldzieher). *Streptothrix Foersteri* held the field until 1894, when the frequent arrangement of the filaments in rays led to identification with actinomyces (v. Schröder, Huth); the star-like arrangement had been noticed earlier by Bajardi (1884) and Tommasoli (1893). Since 1894 numerous cases have been described as actinomycosis (Elschnig, Ewetzki, Lange, v. Schröder, Mitvalski, Robert, Terson, Ginsberg, Mackay).

The benign nature of the affection militates against the diagnosis of actinomyces, but this may be explained by the integrity of the epithelium of the canaliculus; the well-known pleomorphism of actinomyces would account for aberrations from the typical ray figure. In any case

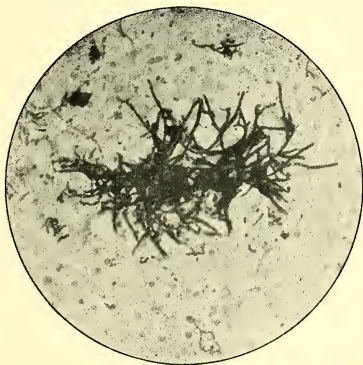


FIG. 546.—STREPTOTHRIX FROM LACRYMAL CONCRETION.
From a photograph by Henderson of a specimen by Mayou.

it is a question of a streptothrix, and the general term had better be employed until the species is definitely determined by culture (Lachner and Sandoval, Axenfeld, Kastalsky). This has hitherto proved impossible or unsatisfactory as regards classification (Axenfeld, Kastalsky), with the exception of Silberschmidt's case, which definitely proves that at any rate, it is not solely a question of actinomyces bovis. Cultures have also been obtained by Dalén, Awerbach, zur Nedden.

Cover-glass preparations of the concretions show a mass of fine filaments, usually without branching, but sometimes with thickened ends; they cannot be distinguished morphologically from leptothrix. The rays characteristic of actinomyces are generally absent. Cultivation is difficult; pure cultures are rarely obtained (Silberschmidt, zur Nedden); usually streptococci and bacilli grow as well (Axenfeld). These soon overwhelm the slow-growing streptothrix in aerobic

cultures. In anaërobic cultures their growth is retarded, and Axenfeld was able in three cases to get the streptothrix to grow (*see* Cahn). In two only was the presence of streptothrix absolutely proved. Similarly Dalén only got the fungus to grow in the deeper parts of the agar puncture; here they formed filaments with sparse branches, and in older cultures marked pléomorphism. Silberschmidt obtained cultures in agar and bouillon; pleomorphism was shown in rods like diphtheria bacilli, some of them branched, in branching filaments with swellings, in short rods and cocco-bacillary forms. Long filaments were seen, but no rays. Inoculations have usually been found to give negative results—intravenous *nil*, intra-peritoneal sometimes abscesses.

Awerbach's case most resembles actinomycosis; cultures inoculated into the peritoneal cavity of a mouse killed in eight days producing typical actinomycotic nodules in the liver and a mesenteric gland.

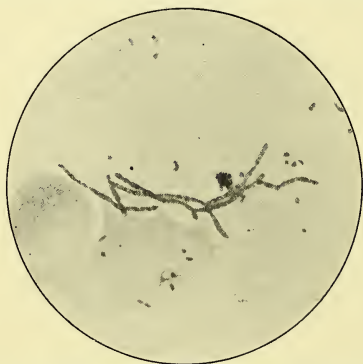


FIG. 547.—STREPTOTHRIX FROM LACRYMAL CONCRETION.

From a photograph by Henderson of a specimen by Mayou. Higher magnification.

Hirschberg and Cannas have reverted to the old diagnosis of leptothrix, chiefly because of the absence of branching. In Cannas' case there were bacilli, cocci, spirilla, and filaments. They stained by Gram, and gave a violet with Lugol's iodine solution. Cultures were obtained on gelatine and glycerine agar; inoculations were negative. *Leptothrix buccalis*, however, never assumes the spirillum form, does not give a positive reaction with iodine, and has never been cultivated in this manner.

*AXENFELD.—In Kolle and Wassermann, *Handb. d. path. Microorg.*, Jena, 1903. v. GRAEFE.—*A. f. O.*, i, 1, 1854; ii, 1, 1855; xv, 1, 1869. GRÜNING.—*A. f. A.*, iii, 1873. COHN.—*Beiträge zur Biologie der Pflanzen*, i, 1878. HIGGENS.—*Brit. Med. J.*, 1879. HAASE.—*A. f. A.*, viii, 1879. v. REUSS.—*Wien. med. Presse*, 1884. GOLDZIEHER.—*C. f. A.*, viii, 1884. v. SCHRÖDER.—*K. M. f. A.*, xxxii, 1894; xxxiv, 1896. HUTH.—*C. f. A.*, xviii, 1894. BAJARDI.—*Jubiläumsch. f. Sperino*, Torino, 1884. TOMMASOLI.—*Giornale ital.*

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INDEX OF ILLUSTRATIONS

(The numbers in brackets refer to the figures, the others to the pages.)

Lids:

1 Plexiform neuroma (528) 733

Cornea:

Anterior staphyloma (282) 408

Hypopyon ulcer (307) 431

Keratectasia (355) 487

Plexiform neuroma (527) 732

Sclerotic:

Plexiform neuroma (527) 732

Sarcoma (364) 502

Tubercle (340) 466

Iris:

Diabetic (302) 425

Epithelium on (298) 420

Necrosis (378) 525

Pupillary membrane (285) 409

Retraction (307) 431, (310) 434,
(343) 471

Synechia:

Anterior (292) 414

Posterior (292) 414

Tubercle (338) 464

Ciliary Body:

Bone in cyclitic membrane (353) 485

Detachment (310) 434

Sarcoma (300) 422, (364) 502

Lens:

Calcareous (343) 471, (355), 487

Cataract:

Anterior capsular (282-3) 408,

(284-5) 409, (286-7) 410, (288)

411, (289) 412, (290-1) 413,

(293-4) 415, (300) 422, (310)

434, (333) 456

Anterior cortical (290) 413

Congenital (291) 413. *See also*

Lamellar

"Dotted" (271) 393

Lens—continued.

Lamellar (278) 401, (279) 402

(280) 403, (281) 404

Morgagnian (277) 399

Posterior cortical (299) 422

Punctate (271) 393

Secondary (296) 419, (297-8)
420, (302) 425

Senile (275) 397, (276) 398

Traumatic (272) 393, (292) 414,
(295) 418

Dislocated (274) 395, (305-6) 431,
(338) 464

Distortion of (301) 423

Epithelium (268) 390

Morgagnian cataract (277) 399

" globules (272) 393,
(273) 394

Shrunken (309) 433, (343) 471,
(355) 487

Suspensory ligament (269-70) 391,
(302) 425

Vitreous:

Connective tissue in (397) 548, (400)
551, (409) 560, (413) 564

Detachment (303-4) 430, (305-6-7)
431

Leucocytes (308) 432, (398) 549,
(399) 550, (413) 564, (414)

565

Choroid:

Angioma (357) 491

Carcinoma (387) 534, (388) 535,
(389) 536, (390) 537, (391) 538,

(392) 539, (393) 540

Choroiditis, acute (327) 446

" disseminated (335-6)
459

Choroid—continued.

- "Colloid bodies" (343) 471, (344) 472, (345) 473, (346) 474, (347) 475, (348) 476, (353) 485, (487) 668
- Degeneration (341) 469, (342) 470, (401) 552, (402) 553, (406) 557, (407) 558, (408) 559, (448) 608
- Fibrous tissue (328) 450, (329) 451, (330) 451, (331) 452, (332) 453
- Hyaline deposits (350) 482, (351) 483
- Membrane of Bruch (324-5-6) 444, (346) 474, (347) 475, (351) 483, (352) 484, (363) 502, (368) 506, (370) 507, (372) 509
- Ossification (349) 481, (350) 482, (351) 483, (352) 484, (353) 485, (354) 486, (355) 487, (356) 488
- Plexiform neuroma (358) 492
- Sarcoma (359) 496, (360) 497, (361) 498, (362) 501, (363-4) 502, (365) 504, (366) 505, (367-8) 506, (369-70) 507, (371) 508, (372) 509, (373-4) 510, (375) 512, (376) 518, (475) 647, (479-80) 649, (481) 650
- Sarcoma, necrotic (378) 525, (379) 526, (380-1) 527, (382) 528
- Sarcoma, flat, diffuse, or infiltrating (383) 529, (384-5) 530, (386) 532
- Supra-choroiditis (332) 453

Retina:

- Angioma (475) 647, (476-7-8) 648
- Cysts (303) 430, (415) 568, (416) 569, (421) 575, (428) 583, (460) 621, (461-2) 623, (463-4) 624, (465) 625
- Degeneration (328) 450, (341) 469, (377) 523, (378) 525, (401) 552, (403) 554, (404) 555, (406) 557, (407) 558, (408) 559, (411) 562, (416) 569, (418) 573, (419) 574, (422) 576, (423) 577, (424) 578, (425) 580, (426) 581, (427) 582, (428) 583, (429) 584, (430) 585, (431-2) 586, (433-4) 588, (435) 589, (436) 590, (438) 592, (440) 594, (441) 595, (443) 603, (444) 604, (445) 605, (446) 606, (447) 607, (449) 608, (451) 611, (460) 621

Retina—continued.

- Detachment (309) 433, (310) 434, (333) 456, (343) 471, (355) 487, (362) 501, (363) 502, (374) 510, (383) 529, (387) 534, (388) 535, (422) 576, (462) 623, (463-4) 624, (465) 625
- Endothelial membrane (418) 573
- Extruded nuclei (395) 543
- Fibrous tissue in (410) 561, (412) 563, (453) 613
- Fœtal (474) 646
- Folding of (330) 451, (331) 452, (420-1) 575, (457) 618, (458) 619
- Giant cells (334) 457
- Glioma (466-7) 628, (468) 629, (469) 630, (470) 631, (471) 632, (472) 636, (473-4) 646
- Hyaline deposits (430) 585
- Medullated nerve-fibres (396) 545
- Melanoma (479-80) 649, (481) 650
- Neuroglia (422) 576, (423) 577
- Normal (394-5) 543
- Œdema (415) 568, (417) 570, (442) 598
- Pigment (331) 452, (437) 591, (438) 592, (439) 593, (440) 594, (441) 595, (443) 603, (444) 604, (445) 605, (447) 607
- Retinitis, acute (327) 446, (442) 598
- pigmentosa (426) 581, (443) 603, (444) 604, (445) 605, (446) 606
- proliferans (450) 610, (451) 611, (452) 612, (453) 613
- Syphilis (454-5-6) 616
- Tubercle (340) 466, (457) 618, (458) 619, (459) 620
- Wounds (397) 548, (398) 549, (399) 550, (400) 551, (401) 552, (402) 553, (403) 554, (404) 555, (405) 556, (406) 557, (407) 558, (408) 559, (409) 560, (410) 561, (411) 562, (412) 563, (413) 564, (414) 565
- Optic Nerve:**
- Artefacts (484) 657
- Atrophy (419) 574, (492) 686, (493) 688
- Corpus amylaceum (485) 660
- Cupping of disc (303) 430, (419) 574, (421) 575, (492) 686, (493) 688
- Hyaline bodies (486) 662

Optic Nerve—continued.

Inflammation (488) 674, (489) 677,
(490) 680

Medullated nerve-fibres (396) 545

Normal (482) 653, (483) 655

Tubercle (491) 684

Tumours (500-1) 694, (502-3) 695,
(504-5) 696, (506-7-8-9) 697,
(510) 698, (511) 700, (512) 701,
(513-4) 702, (515-6) 703, (517)
704, (518) 705, (519) 706,
(520-1) 709, (522) 714, (523)
715

Vascular degeneration (494-5-6-7)
691, (498-9) 692

Orbit :

Cysts (524) 717, (525) 718, (526)
719

Plexiform neuroma (527) 732, (528)
733, (529-30) 734, (531) 735,
(532) 736

Osteoma (537-8) 746

Sarcoma (533) 741, (534) 742, (535)
743, (536) 744

Lacrymal Apparatus:

Concretions (546) 759, (547) 760

Dacryops (539) 751

Tumours of lacrymal gland (540)
754, (541-2-3) 755, (544-5) 756

General :

Cholesterin (334) 457, (369) 507,
(371) 508

Cysticercus (311-2-3) 436-7

Hyaline deposits (350) 482, (351)
483, (430) 585, (486) 662

Hyaline membrane (294) 415

Hydatid (314-23) 438-41

Liver, metastatic sarcoma (360) 497

Lung, carcinoma (390) 537

Panophthalmitis (308) 432, (327)
446

Phthisis bulbi (310) 434, (343) 471

Rib, metastatic carcinoma (361) 498

Ruptured globe (306) 431

Vascular degeneration (342) 470,
(377) 523, (433-4) 588, (435)
589, (436) 590, (454-5-6) 616,
(494-5-6-7) 691, (498-9) 692

INDEX

(Where there are several references the most important is printed in *italics*.)

- Actinomycosis, 759
- "After-cataract," 419
- Angioid streaks, 585
- Angioma of choroid, 490
 - of lacrymal gland, 753
 - of optic nerve, 711
 - of orbit, 725
 - of retina, 651
- Angiosarcoma of choroid, 505
 - of retina, 651
- "Apparent cataract," 400
- Artefacts of lens, 392
 - of optic nerve, 657
 - of retina, 546
- Arteriosclerosis, 469, 587, 690
- Aspergillus in vitreous, 434
- Atrophia bulbi, 434
 - in glioma, 524, 529
 - in sarcoma of choroid, 642, 644
- Atrophia gyrata choroideæ et retinæ*, 605
- Atrophy of choroid, 468
 - of retina, 577
 - optic, 686
 - primary, 689
 - secondary, 686
- Bacteriology of dacryocystitis, 757
 - of septic retinitis, 600
- "Bläschenzellen," "Blasenzellen," 398
- Bruch's membrane, 445, 478
- Calcification, 427, 480, 517, 523, 587, 634, 635
- Canaliculi, normal, 749
 - concretions in, 758
- Carcinoma of choroid, 533
 - of lacrymal gland, 752
- Cartilage in choroid, 489, 503
 - in lacrymal gland growths, 754
 - in orbital growths, 730, 745
- Cataract, 392
 - "after-," 419
 - anterior capsular, 407, 423
 - — cortical, 407, 413, 423
 - — polar, 407
 - "apparent," 400
 - axial, 402
 - black, 400
 - central, 404
 - complicated, 421
 - diabetic, 425
 - fusiform, 402
 - hypermature, 400
 - in general, 392
 - lamellar, 401
 - Morgagnian, 400
 - naphthalin, 424
 - nuclear, 404
 - perinuclear, 401
 - posterior cortical, 417, 423
 - — polar, 417
 - punctate, 400
 - pyramidal, 414
 - secondary, 419, 421
 - senile, 398
 - special forms, 398
 - total congenital, 404
 - toxic, 424
 - traumatic, 417
 - zonular, 401
- Cataracta nigra, 400
 - senilis præmatura punctata, 400
- Chloroma, 729

- Cholesterin in glioma, 634
 - in lens, 395
 - in sarcoma of choroid, 508
 - in subretinal fluid, 457
 - in vitreous, 429
 - tests for, 457
- Chondrosarcoma of orbit, 745
- Choriocapillaris, 445
- Choroid, degenerations, 468
 - inflammation, 446
 - normal, 443
 - ossification, 480
 - tumours, 489
 - wounds, 445
- Choroiditis, acute, 446
 - chronic, 449
 - disseminated, 458
 - exudative, 449
 - hyperplastic, 450
 - metastatic, 448, 460
 - nodular, 449, 460, 467
 - subacute, 449
 - suppurative, 446
 - sympathetic, 460
- Choroido-retinitis, 446, 607
- "Chromatophoroma," 519
- Cicatrisation in retina, 564, 614
- Circle of Zinn, 653
- "Colloid bodies," 470, 489, 605, 661
- Concretions in canaliculi, 758
- Congenital cataract, 401
 - cysts of orbit, 716
 - tumours, 489, 626, 693, 726, 728, 730, 732
- Corpora amylacea, 659
 - arenacea, 706
- Cylindroma of orbit, 743
- Cysticercus, intra-ocular, 436
 - orbital, 724
- Cysts, acquired, 722
 - congenital, 716
 - cysticercus, 436, 724
 - dermoid, 716
 - hydatid, 438, 723
 - implantation, 722
 - inclusion, 721
 - parasitic, 436, 723
 - serous, 722
 - teratoid, 716
 - of the lacrymal gland, 751
 - of the orbit, 716
 - of the retina, 569, 583, 621, 623
- "Cytoid bodies," 552, 578
- Dacryocystitis, 757
- Dacryops, 751
- Degeneration, calcareous, 480, 517, 523, 587, 634, 635
 - fatty, 517, 586, 595, 633
 - hyaline, 468, 470, 516, 587, 635, 661, 693
 - myxomatous, 516, 700, 714, 728, 744, 745, 754
 - vascular, 469, 587, 615, 670, 685, 690
- Degenerations of choroid, 468
 - of lens, 392
 - of optic nerve, 685
 - of retina, 567, 577
- Dermoid cysts of orbit, 716
 - of choroid, 489
- Detachment of retina, 434, 522, 623, 639
 - — — early, 522
 - of vitreous, 429
- Diabetic cataract, 425
- Diffuse sarcoma, 494, 529
- "Diktyoma," 647
- "Drusen," 661
- "Early detachment of retina," 522
- Echinococcus, 438, 723
- Elastic tissue of choroid, 443
 - — of optic nerve, 655, 659
 - — of retina, 546
- Elephantiasis neuromatodes, 692, 730
- Encephalocele, 721
- Endothelial membranes, 429, 550, 572
- Endothelioma, interfascicular, 520
 - of choroid, 505, 520, 531
 - of lacrymal gland, 752
 - of optic nerve, 693, 704
 - of orbit, 738
- External limiting membrane, 542
- Extra-dural tumours, 704
- Extruded nuclei, 543
- Fatty degeneration, 517, 586, 595, 633
- "Fettkörnchenzellen," 678, 688
- Fibrogia, 757
- Fibroma of optic nerve, 699
 - of orbit, 728
- "Fibromatosis," 700, 709
- Fibro-sarcoma of choroid, 494
 - of lacrymal gland, 753
 - of optic nerve, 699, 705
 - of orbit, 739
- Fibrous degeneration of retina, 576
- Filariae, 421, 441, 725

- Flat sarcoma, 494, 529
 Fluidity of vitreous, 429
 Folding of retina, 452, 576
 Fovea centralis, 546
 — externa, 546
 Ganglion cells, 544
 — — in glioma, 632
 Giant-celled sarcoma of orbit, 741
 — cells in dermoid cysts, 719
 — — in sarcoma of choroid, 503. *See also*
 Tubercle
 Glaucoma in glioma retinae, 627
 — in sarcoma of choroid, 498, 523, 529
 Gliangiosarcoma, 629
 Glioma retinae, 626
 — — cytology, 630
 — — degeneration, 633, 635
 — — endophytum, 627, 637, 639
 — — exophytum, 627, 637, 639
 — — frequency, 626
 — — histogenesis, 645
 — — in anterior chamber, 641
 — — in choroid, 640
 — — in ciliary body, 641
 — — in cornea, 641
 — — in iris, 640
 — — in lens, 421, 641
 — — in optic nerve, 644
 — — in sclerotic, 641
 — — in vitreous, 435, 639
 — — metastasis, 638
 — — origin and propagation, 636
 — — retrogression, 644
 — — rosettes, 631
 — — structure, 627
 — — vessels, 635
 — — with atrophía bulbi, 642
 Gliosarcoma of optic nerve, 699
 — of orbit, 740, 745
 "Gliosis of retina," 576
 Glycogen, 516
 Gumma : *see* Syphilis
 Hæmangioma of choroid, 490
 — of orbit, 726
 — of retina, 651
 Hæmorrhage in carcinoma, 538
 — in retina, 571, 599, 600, 609
 — in sarcoma, 517, 528, 741
 — in vitreous, 435, 609
 — in wounds of retina, 559
 — subchoroidal, 453
 Hæmosiderin, 515
 Haller's layer, 443
 Henle's fibres, 543, 569
 Holes in retina, 583
 Hyaline bodies at optic disc, 661
 — degeneration, 468, 470, 516, 587, 635.
 661, 693, 744, 754
 — deposits in retina, 585
 — membrane, new-formed, 411, 414
 "Hyalitis," 428, 435
 Hydatid cysts, 438, 723
 Hydro-encephalocele, 721
 Implantation cysts of orbit, 722
 Inclusion cysts of orbit, 721
 Indirect Wallerian degeneration, 673, 687
 Inflammation of choroid, 446
 — of lacrymal sac, 757
 — of optic nerve, 673
 — of retina, 568
 "Intercalated tissue," 657
 "Interstitial tissue," 655
 Intra-dural tumours, 693
 Irido-cyclitis in glioma retinae, 644
 — in sarcoma of choroid, 524, 526, 529
 Iron in lens, 421
 — in pigment, 515, 572
 — tests for, 515
 Iwanoff's cysts, 621
 Lacrymal apparatus, 749
 — gland, cysts of, 751
 — — normal, 749
 — — tumours of, 752
 — sac, inflammation, 757
 — — normal, 750
 Lamellar cataract, 401
 Lamina cribrosa, 655
 — supra-choroidea, 443
 Lange's fold, 546
 Lens, calcification, 427
 — foreign substances in, 421
 — normal, 389
 — ossification, 427
 — size of, 390, 405. *See also* Cataract.
 Leprosy, 424, 467, 621, 685
 Lepto-meningitis, 680
 Leptothrix, 758
 Leucosarcoma of choroid, 493, 517
 Leukæmic tumours of the orbit, 729
 "Limiting tissue," 656
 Lipoma of orbit, 727

Lymphangioma of orbit, 727
 Lymphangio-sarcoma of choroid, 509, 520
 Lymphoma of lacrymal gland, 753
 — of orbit, 728

 Macula lutea, 546
 Medullated nerve-fibres, 544, 579, 654
 Melanin, 514
 Melanoma of retina, 651
 Melanosis, 493, 523
 Meningocele, 721
 "Meniscus" of optic nerve, 656
 Metaplasia, 520
 Metastasis in glioma retinae, 638
 — in sarcoma of choroid, 499
 — — of orbit, 740
 Metastatic choroiditis, 446, 448
 — retinitis, 598
 Morgagnian cataract, 400
 — globules, 394
 Müller's fibres, 545
 Myeloid sarcoma of orbit, 741
 Myoma of choroid, 490
 Myxomatous degeneration, 516, 700, 714
 Myxosarcoma of optic nerve, 699
 — of lacrymal gland, 753
 — of orbit, 740, 744

 Nasal duct, 750
 Necrosis in carcinoma, 538
 — in glioma retinae, 629, 633
 — in sarcoma of the choroid, 525
 Neuritis, optic, 673
 — — in optic-nerve tumours, 708
 — — metastatic, 682
 Neuro-epithelioma, 646
 Neuro-fibromatosis, 492, 730
 Neuroglia in glioma, 633
 — of optic nerve, 654, 658, 679
 — of retina, 545, 576, 582
 Neuroglial mantle, 658
 "Neuroglioma ganglionare," 646
 Neuroma, 699
 — of orbit, 730
 — plexiform, 492, 730
 Nodular choroiditis, 449, 460, 467

 Œdema in growths, 700, 714, 728, 744
 — of choroid, 446
 — of optic nerve, 674
 — of retina, 568
 Opaque nerve-fibres, 544, 579, 654
 Optic nerve, blood-vessels, 659

Optic-nerve, corpora amylacea, 659
 — — degenerations, 685
 — — "Drusen," 661
 — — hyaline bodies, 661
 — — inflammation, 673
 — — normal, 652
 — — tumours, 693
 — — wounds, 672
 Orbit cysts, 716
 — tumours, 725
 Ossification in choroid, 480
 — in lens, 427
 — in retina, 587
 — in vitreous, 442
 Osteoma of orbit, 745
 Osteosarcoma of choroid, 494
 — of orbit, 741, 746

 Pachymeningitis, 680
 — chronica, 682
 Panophthalmitis, 432, 446, 597, 674
 Papillitis, 674
 Parasites, 421, 436, 441, 723
 "Pericystitis," 758
 Perineuritis, 680
 "Peripheral atrophy of optic nerve," 658
 Perithelioma, 520, 651
 "Phakitis," 392
 Phthisis bulbi, 434
 — — in glioma retinae, 642, 644
 — — in sarcoma of choroid, 524, 529
 Physaliphores, 434
 Pigmentation, autochthonous, 511, 514
 — hæmatogenous, 511, 514
 — of orbital tumours, 741
 Pigment epithelium in glioma retinae, 634, 639
 — — in sarcoma of choroid, 513
 — — normal, 542
 — — pathological, 591, 602, 607
 Plexiform neuroma, 492, 730
 Plica centralis, 546
 Pneumococci, 600, 757
 Psammoma, 711
 Pseudoglioma, 455, 466
 Pseudo-leukæmic tumours of orbit, 729
 Puncta lacrymalia, 749
 Punctate cataract, 400
 Pyramidal cataract, 414

 Retention cysts of lacrymal gland, 751
 Retina, cysts, 569, 621
 — degeneration, 577
 — detachment, 434, 522, 623, 639

- Retina, inflammation, 568
 — normal, 542
 — œdema, 568
 — tumours, 626
- Retinitis, 597
 — circinata, 600
 — metastatic, 598
 — pigmentosa, 602
 — "plastic," 614
 — proliferans, 609
 — purulent, 597
 — septic, 597
 — septica (Roth), 599
- Ring sarcoma, 494, 529
- Rosettes, 631
- Sarcoma carcinomatoides, 505, 743
 — in lens, 421
 — in vitreous, 435
 — metastatic, 533
 — of choroid, ætiology, 496
 — — classification, 493
 — — course, 498
 — — cytology, 495, 501, 530
 — — degeneration, 516
 — — frequency, 494
 — — histogenesis, 517
 — — metastasis, 499
 — of lacrymal gland, 753
 — of optic nerve, 693, 704
 — of orbit, 738
 — — primary, classification, 738
 — — — cytology, 740
 — — — frequency, 739
 — — — metastasis, 740
 — — — pigmentation, 741
 — — — structure, 742
 — — — varieties, 744
 — — secondary, 745
- "Sarcome en nappe, en plaque," 424, 529
- Sattler's layer, 443
- Scirrhous of lacrymal gland, 752
- Secondary cataract, 419, 421
- Senile cataract, 398
 — changes in choroid, 468
 — — in lens, 392
 — — in optic nerve, 685
 — — in retina, 596
- Serous cysts of orbit, 722
- Streptococci, 448
- Streptothrix, 759
- Suprachoroiditis, 453
- Suspensory ligament, changes in, 426
 — — normal, 389
- Sympathetic ophthalmia, 460, 524, 527
- Synchysis scintillans, 429
- Syphilis of choroid, 458, 461
 — of optic nerve, 683
 — of retina, 615
- Tapetum, 443
- Telangiectasis of choroid, 490
 — of orbit, 726
- Teratoid cysts of orbit, 716
- Toxic cataracts, 424
- Toxins, 448, 526
- Trachoma affecting choroid, 467
- Traumatic cataract, 417
- Tubercle, chronic, 465
 — conglomerate, 466
 — miliary, 463, 683
 — of choroid, 462
 — of optic nerve, 683
 — of retina, 617, 683
 — solitary, 466
- Tumours of choroid, 489
 — of ethmoid, 748
 — of frontal sinus, 747
 — of lacrymal gland, 752
 — of optic nerve, 693
 — of orbit, 725
 — of retina, 626
 — of sphenoid, 748
- Varicose nerve-fibres, 546, 552, 579, 702
- Vascular degeneration in choroid, 469
 — — in optic nerve, 635, 690
 — — of retina, 587, 615
- Vesicular cells, 398
- Vitreous, abnormal products in, 432
 — detachment, 429
 — fluidity, 429
 — hæmorrhage, 435, 609
 — in glioma, 639
 — normal, 428
 — parasites, 436
- Wounds of choroid, 445
 — of optic nerve, 672
 — of retina, 547
- Zinn, circle of, 653
 — zonule of, 389, 426
- Zonular cataract, 401
- Zonule of Zinn, 389, 426

